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SCIENTIFIC AMERICAN **MIND**

THOUGHT • IDEAS • BRAIN SCIENCE

June/July 2006

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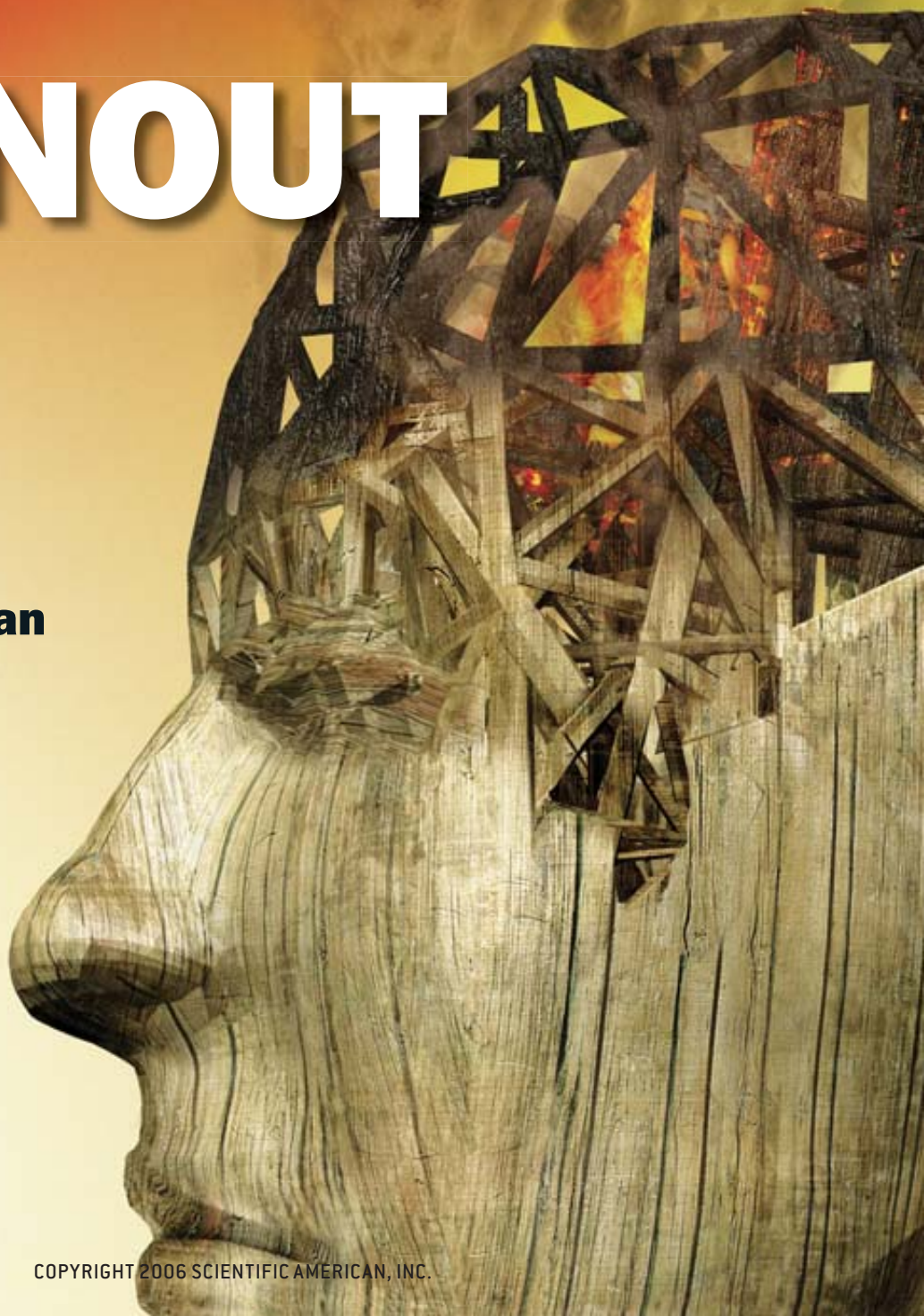
How **Thoughts** Flow

The Mind of **Rain Man**

Controlling **Epilepsy**

Bitter Gets Better

Crossing the Brain's
Drug Barrier



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SCIENTIFIC AMERICAN MIND

THOUGHT • IDEAS • BRAIN SCIENCE

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*Many of the articles in this issue
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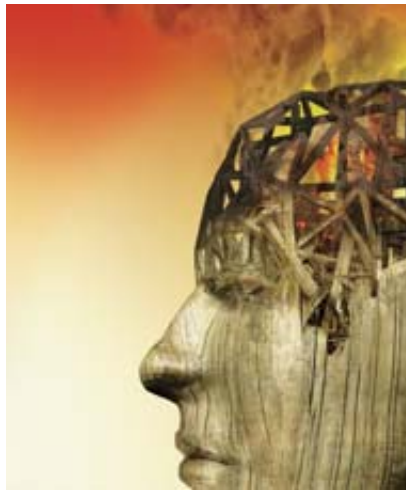
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Feel the Burn

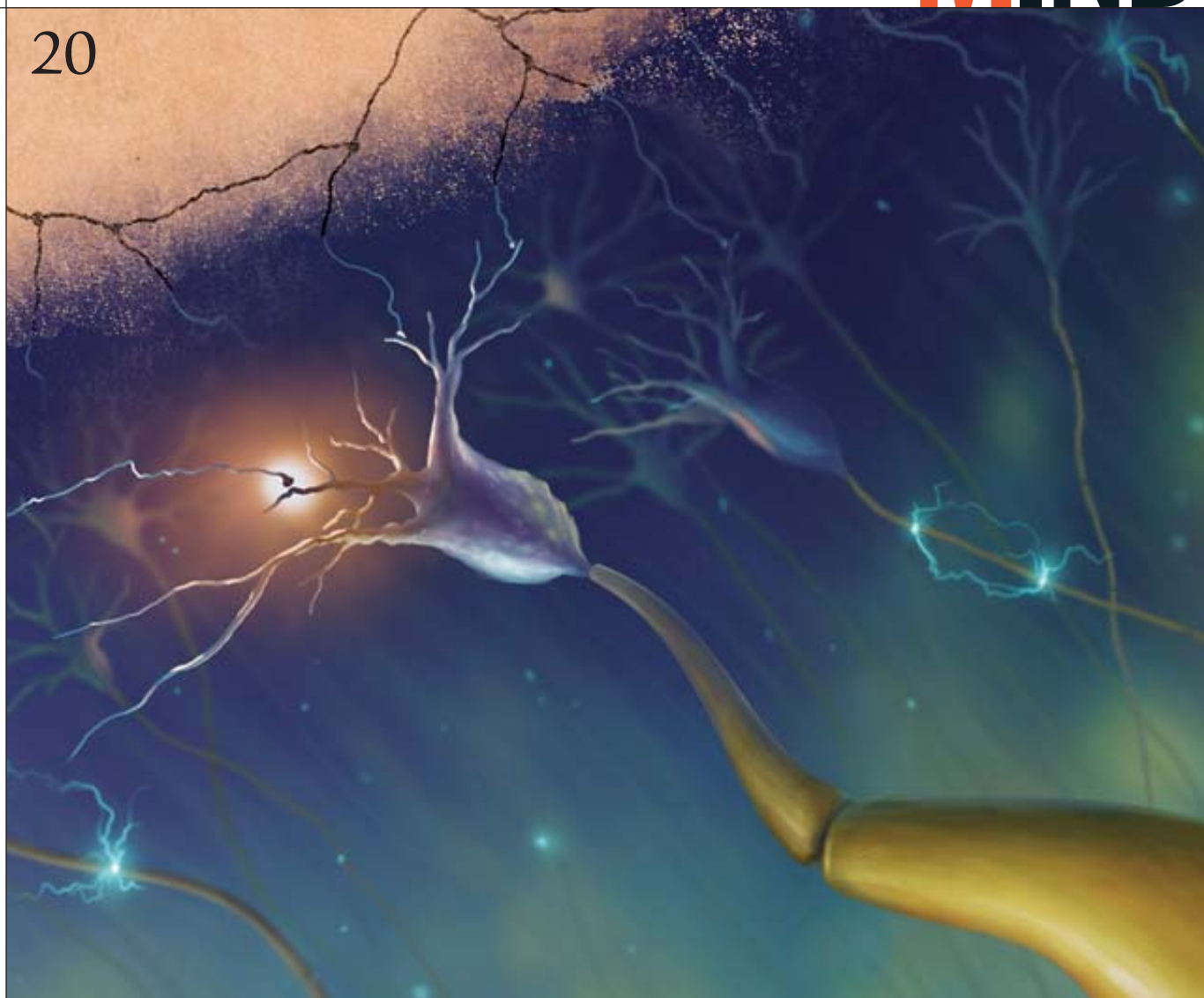
Bounding down the stairs to my health club's locker room at lunch today, I spied a new poster that caught my attention: "Leave your stress where it belongs: in your cubicle!" Usually I roll my eyes at marketing exhortations, but this time I had to agree that the writers had a point. In an era of lean staffing and multitasking, workers are at greater risk of making themselves sick from long-term stress, as Ulrich Kraft explains in his article "Burned Out." Workaholics who pull long hours year in and year out can drive themselves to a state of mental and physical collapse, called burnout. Fortunately, there are ways for the brain and body to ward off such dire consequences. Turn to page 28 to find out how.

Tension can be beneficial, of course, if it is part of the time-tested system of improving explanatory arguments, or interpretations, based on experimental data. Such debates advance science's pursuit of discovering the truth about any given phenomenon. In "Beyond the Neuron Doctrine," starting on page 20, neuroscientist R. Douglas Fields describes a century-old question about the nature of neural communication. One side contends that each brain cell is a discrete functional unit, a scheme now known as the neuron doctrine. The opposing view holds that the nervous system is a highly interconnected, free-flowing data meshwork, or reticulum. The surprising news? Both camps are right.

As the neuron debate shows, hardly any matter is a simple, black-or-white issue. Especially not our perception of those two polar opposites, the colors black and white themselves. Psychologist Alan Gilchrist relates how the brain deciphers the often contradictory and confusing visual inputs that we receive from our surroundings. Scientists "ask" the brain about its thinking by showing volunteers striking optical illusions, some of which you will see in Gilchrist's article "Seeing in Black and White," beginning on page 42. Such research may be one of the few instances in which the routine use of deceptions serves the greater good of revealing reality.

Mariette DiChristina
 Executive Editor
 editors@sciam.com

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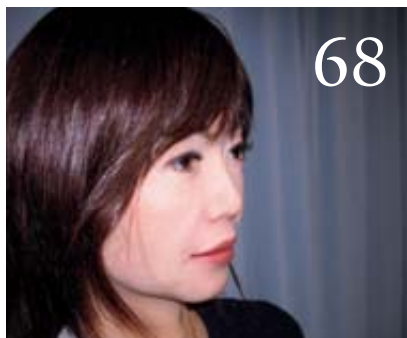
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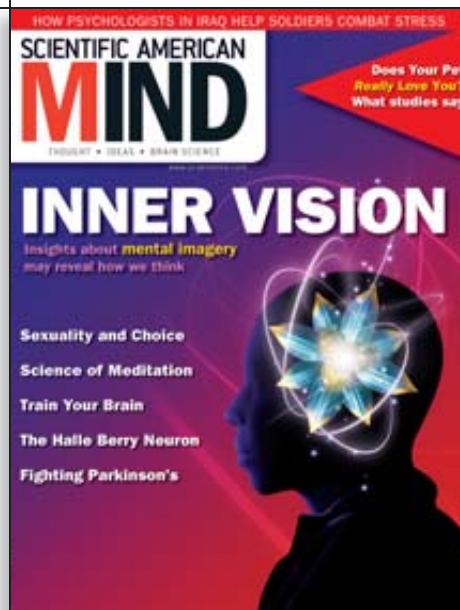
BY ABBIE F. SALNY

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"EACH TIME YOU THINK you are unveiling the truth, all you get is a teasing glimpse of what turns out to be yet another veil," wrote Vilayanur S. Ramachandran and Diane Rogers-Ramachandran in their February/March Illusions column ["Stability of the Visual World"]. Their words eloquently capture the stubborn persistence of researchers as they grapple with seemingly impenetrable mysteries of the mind.

Along the same lines, articles in the issue discussed the struggle to understand how mental imagery forms ["Picture This," by Thomas Grueter], how sexuality can vary ["Do Gays Have a Choice?" by Robert Epstein], whether our fellow creatures emote ["Do Animals Have Feelings?" by Klaus Wilhelm] and more.



INNER WORLDS

I very much enjoyed the article "Picture This," by Thomas Grueter. He is correct in asserting that the general debate about the nature of mental imagery still continues. (For the latest update, see the book I wrote with William L. Thompson and Giorgio Ganis called *The Case for Mental Imagery*, Oxford University Press, 2006.) He is incorrect, however, regarding the specific debate regarding brain activation.

The two major contending camps, in Caen (France) and Cambridge (U.S.), independently converged on the same account for inconsistent findings: different types of mental imagery rely on different brain networks. In particular, the brain network that underlies imagery for spatial relations (as in imagining an object rotating) relies crucially on the parietal lobes, whereas the network that underlies imagery for high-resolution shapes relies crucially on the occipital lobes. Even so, key areas in each of these networks are organized so that a picturelike pattern of activation is evoked during imagery.

As far as the brain is concerned, mental images are in fact images—not merely descriptions.

Stephen M. Kosslyn

John Lindsley

Professor of Psychology
in Memory of William James
Harvard University

Grueter is correct that "the final word on mental imagery has not yet been uttered." What seems to be missing from both schools of thought—the descriptionists and the pictorialists—is how their image mechanisms link to the inner worlds of nonhuman species. Human neural processes are extraordinary, but they are not completely unique, having evolved with many operational features of other animals. Conversely, animals conduct their daily business based strictly on imagery, without any access to stored symbolic references as we know them.

To get at the kernel of the human imagery question, we need to explain how animals create internal images without abstractions like language or grammatical structures.

David Werdegarr

Naperville, Ill.

RANGE OF SEXUALITY

In Robert Epstein's "Do Gays Have a Choice?" I was glad to see people speaking up against the excluded middle arguments inherent in the "nature versus nurture" and even the "straight versus gay" views. There are, however, a couple of notable absences in the article.

First, why no mention of Evelyn Hooker? In 1957 Hooker administered projective tests such as the Rorschach test to 30 straight and 30 gay

men and then had experts evaluate their adjustment levels. The results for the two groups were essentially identical, and when the experts were asked to identify which results came from heterosexuals and which from homosexuals, their interpretations fared no better than chance. Surely this study and the ones that followed it had an impact on the American Psychiatric Association's decision to remove homosexuality from the *Diagnostic and Statistical Manual*.

Second, whereas there is much print given to Robert L. Spitzer's study presented to the APA in May 2001, why no report about a paper presented at the same convention by Ariel Shidlo and Michael Schroeder? In their study 202 homosexuals who had undergone conversion therapy were interviewed, and 88 percent stated they felt that the efforts to change their sexual orientation had failed.

David Hardison

Denver

As someone who has always believed that sexuality exists in a spectrum, I found "Do Gays Have a Choice?" to be a delight. But the quiz left me with a sour aftertaste. I come out as being "predominantly homosexual." This result came about because all the questions were regarding having feelings for, or doing some-

thing with, a person of the same sex, and the questions were not balanced with the same for the opposite sex.

My younger years were filled with experiences with both sexes. Still now, at 26, I have feelings for the same sex. Yet I am married to someone of the opposite sex, even though in the country where I come from same-sex marriage is legal. My decision was not made for procreational purposes, because I knew before the relationship that I could not have children. Nor

test—the Epstein Sexual Orientation Inventory—from which the mini test was derived, measures both gay and straight tendencies, reports one's Mean Sexual Orientation, and also gives one's Sexual Orientation Range, which is a measure of choice and flexibility. It is accessible at <http://mysexualorientation.com>

POWER OF PLEASURE

It speaks volumes about the inherent conservatism of science that we should still be asking the question, as

for a review of the letter writer's book.]

Jonathan Balcombe
Physicians Committee for
Responsible Medicine
Washington, D.C.

A SCIENTIFIC APPROACH

In his review of *Fool's Paradise: The Unreal World of Pop Psychology*, Kenneth Silber wonders at the continuing popularity of self-help books. Perhaps one answer might be found in the shortcomings of *professional* psychological help.

As *Scientific American Mind* itself has reported, the psychology profession has a tendency to cling to unproved and even disproved practices and theories such as MBTI, Rorschach tests or repressed-memory recovery. If practitioners relied on scientific and evidence-based foundations, perhaps then we would be able, as Scott Adams (creator of cartoon character Dilbert) once satirically suggested, to replace the bookstore's entire "Self-Help" section with a sign that reads: "Go read any book in the History, Philosophy, or Religion section and think about what it says."

Carl Zetie
Waterford, Va.



Animals may experience emotions such as joy, sympathy, fear and grief.

was it done because of social pressure, because I had not had any bad experiences while in a same-sex relationship before my marriage. Opposite-sex relationships have never made me feel uncomfortable or like a lie. Nor have same-sex relationships felt like the "truth."

I am happy and comfortable with either sex, both as friends and sexual partners. There is a name for this midpoint on the continuum: bisexual. This middle ground seems to have been totally overlooked in the questions.

Ineke Warner
U.K.

EPSTEIN REPLIES: The quiz included with the article is indeed quite skewed, intended to bring out the homosexual side of people's natures, which is why it is called "How Gay Are You?" The full

author Klaus Wilhelm does, "Do Animals Have Feelings?" The weight of evidence—from the fact that emotions are adaptive to the way animals respond behaviorally and physiologically to emotive stimuli—leaves no reasonable doubt that they do. Part of the problem is that science has been too mired in seeking evolutionary explanations for animal behavior, to the neglect of an individual's experience. Mate-seeking minks and romping ravens do not contemplate Darwinian fitness or reproductive success: they are drawn to behave adaptively because of the rewarding feelings it brings.

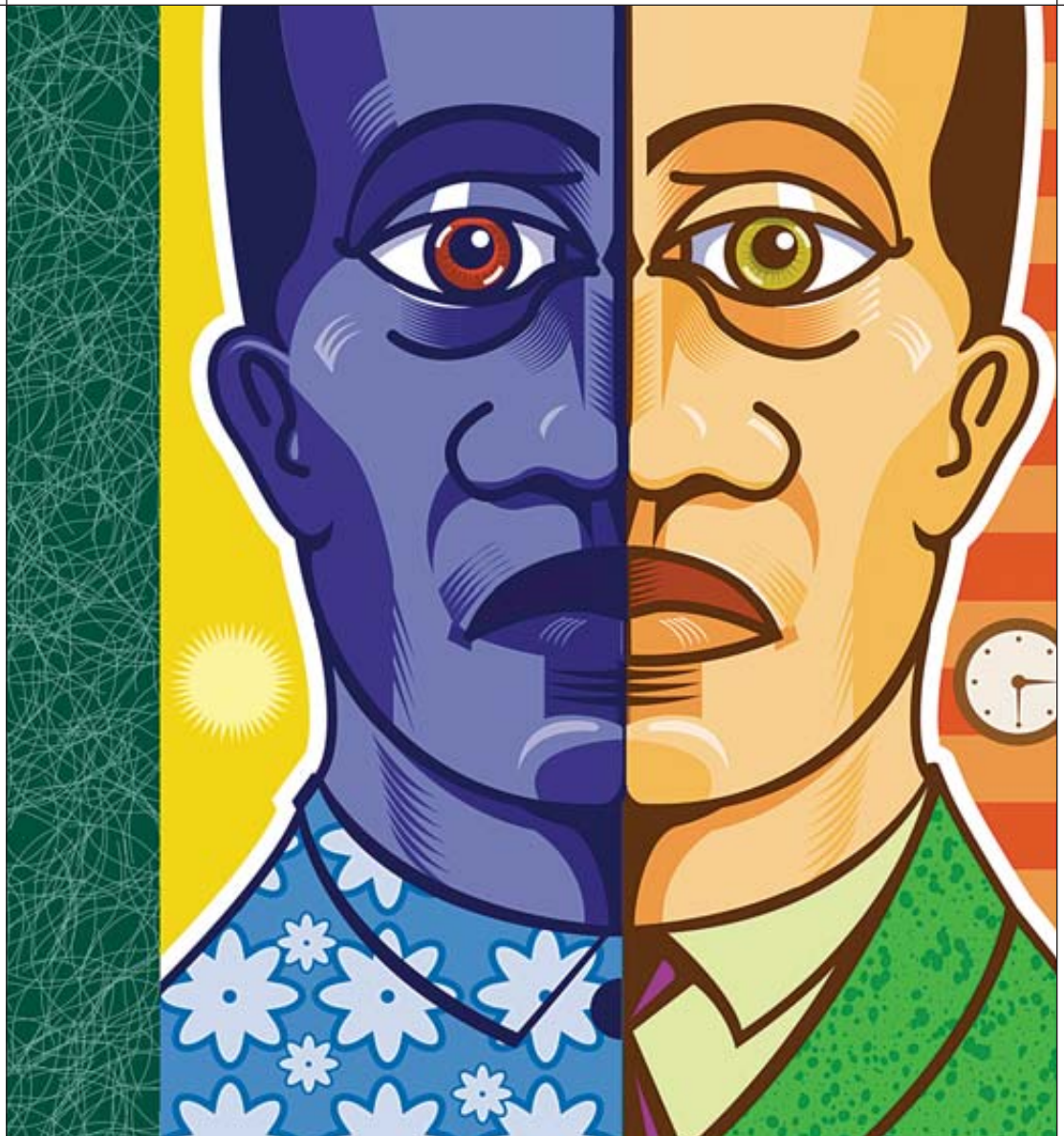
As I argue in my book *Pleasurable Kingdom: Animals and the Nature of Feeling Good* (Macmillan, 2006), we would do well to take more notice of the power of pleasure in motivating behavior. [Editors' note: See page 82

ERRATA "Train Your Brain," by Ulrich Kraft, mistakenly placed Neuro-Quest Ltd. in Evanston, Ill.; it is in Skokie, Ill. Also, it reported that, "Whenever the amplitude of alpha waves in the left frontal cortex rose above that in the right, the participants would hear a pleasant note played on a clarinet." The opposite is true: Whenever the amplitude of alpha waves in the *right* frontal cortex rose above that in the *left*, the participants would hear a pleasant note played on a clarinet.

In "Stability of the Visual World," by Vilayanur S. Ramachandran and Diane Rogers-Ramachandran [Illusions], the graphic entitled "Movement Detectors" was mislabeled. The labels for "the feed-forward theory (top)" and for "the feedback theory (bottom)" should have been reversed.

Send letters to editors@sciammind.com

Head Lines



Two Languages, Two Minds

Many bilingual individuals say they feel like a different person depending on which language they are speaking. A new study lends credence to their claims.

Nairán Ramírez-Esparza, a psychology doctoral student at the University of Texas at Austin, charted the personality traits of 225 Spanish/English bilingual subjects in both the U.S. and Mexico as they responded to questions presented in each language. Ramírez-Esparza and her colleagues found three significant differences: when using English, the bilinguals were more extraverted, agreeable and conscientious than when using Spanish.

Researchers have shown before that bicultural individuals can assume different roles depending on environmental cues. But the new results indicate that character itself can morph.

“To show that changes in personality—albeit modest ones—can be triggered by something as subtle as the language you’re speaking suggests that personality is more malleable than is widely expected,” Ramírez-Esparza says. Switching tongues will not turn a bookworm into a party animal, but the variances are noticeable nonetheless.

The investigators ruled out differences between translations of the questions as possible confounding factors, and all subjects were truly fluent. “The results are significant in that they document the contextual nature of personality,” says Daniel Heller, a psychology professor at the University of Waterloo in Ontario not involved in the research. “The U.S. is becoming increasingly bicultural and bilingual,” Ramírez-Esparza points out, “so it is important that we start to develop a better understanding of bicultural minds.”
—Matthew Hutson

GETTY IMAGES

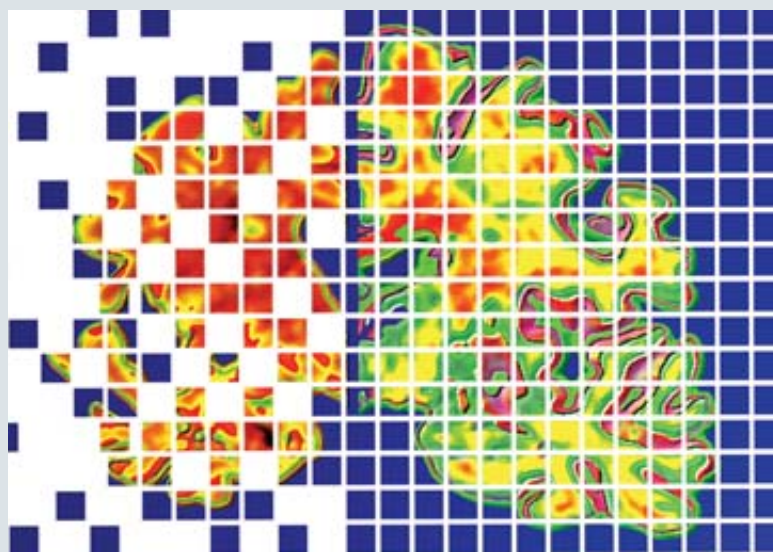
Trace of Alzheimer's

A new radioactive tracer may one day be used to predict whether a person might develop Alzheimer's disease.

The brains of Alzheimer's sufferers are usually shot through with plaques of the protein beta amyloid and so-called tangles of a protein known as tau. Radioactive tracers for beta amyloid plaques exist, but they do not fully distinguish healthy from diseased tissue, says Gary Small, a geriatric psychiatrist at the University of California, Los Angeles. Small and his colleagues conducted positron-emission tomographic scans using a synthetic radioactive compound, FDDNP, that sticks to plaques and tangles. They scanned 60 people, some of "normal" mental status and some with mild cognitive impairment or Alzheimer's. The greater an individual's cognitive problems, the more the tracer showed up in the brain, in certain signature patterns.

In follow-up scans of 12 individuals two years later, those whose mental abilities had deteriorated showed greater accumulation of the tracer, suggesting a possible predictive value. The results are encouraging for diagnosing Alzheimer's and forecasting its progression, says neuroscientist Mony de Leon of New York University. Predicting the onset of the disease may be more complicated, however, because researchers do not know the behavior of plaques and tangles in healthy people or those with other disorders. Siemens AG has licensed FDDNP and is evaluating the technique's forecasting power, Small says.

Other experiments are identifying factors that could help



Prediction of tissue loss (represented symbolically at left) is improving.

predict the pace of illness. For example, Nikolaos Scarmeas of Columbia University and his colleagues recently reported on 312 newly diagnosed Alzheimer's patients whom they followed for an average of six years. The more years of formal schooling the patients had, the faster their memories declined—strengthening the conclusion of less comprehensive studies, Scarmeas says. Although more highly educated people succumb to Alzheimer's later in life—perhaps because they can more easily compensate for initial impairments—the results indicate the delay may come at the cost of having less in reserve to slow progression once the disease finally kicks in, Scarmeas explains.

—JR Minkel

Quick, How Many?

Scientists estimate that 3 to 6 percent of the population may be unable to count objects quickly. By isolating the brain's counting region, they are figuring out just how people calculate the number of items present.

The problem in identifying the precise region is that counting typically involves language, and the language areas also come online when the brain enumerates. To keep them offline during experiments, postdoctoral researcher Fulvia Castelli of the California Institute of Technology used colors. That was when she found that the intraparietal sulcus—a long sliver of tissue in the back of the brain—tabulates how many and not how much. Volunteers were shown a series of blue and green flashes of light filling rectangles on a video chessboard. When the colors appeared in isolated squares the sulcus was activated, but

when the colors were strung together in a row it was not.

A real-life analogy might be deciding quickly which checkout line at a grocery store is shorter. Some people tote up the individuals standing in line, others create a mental representation of how long the queue actually is. People with "dyscalculia" cannot develop that mental map, forcing them into slow, deliberate tallying. Castelli hopes to study ways to strengthen the representational ability.

—Jamie Talan



Meetings Are Great

Most people would say that employees hate office meetings. “It’s one of those anecdotal things that’s hard to question,” says organizational psychologist Steven G. Rogelberg of the University of North Carolina at Charlotte. But when Rogelberg and his colleagues gave 980 workers one of two questionnaires about their time spent in scheduled meetings and overall job satisfaction, the get-togethers were not uniformly panned.

Employees who are goal-oriented and whose work does not require much outside input do indeed tend to be generally dissatisfied with meetings. But individuals whose work depends on interaction with others and who have somewhat flexible, unstructured jobs are actually more satisfied the more gatherings they sit in on. “I think it’s a social norm to complain about your meetings,” Rogelberg observes. —JR Minkel



See It, Grab It

When you open your eyes and reach out to shut off the alarm clock, two distinct brain systems are activated: one recognizes the clock, and the other guides your hand. Neuroscientists have long been aware of this “dissociation” between the recognition and guidance systems, but they had not been able to observe both in action. Now Lior Shmuelof and Ehud Zohary of Hebrew University in Jerusalem have used functional magnetic resonance imaging to see the duality in action in human volunteers.

The subjects watched videos of hands entering the screen from one side and grasping objects on the opposite side. Most previous studies of the two visual systems, Shmuelof explains, “were of people who had had brain damage. Those suffering from agnosia could not recognize objects, whereas those with ataxia could identify objects but could not guide their hands to grab them.” He says his work with Zohary is the first to test individuals for whom both systems operate normally.

“Our study confirmed that there are two systems,” Shmuelof says, “but it also found that this model is too simple. Some parietal brain regions, associated with planning to grasp objects, are also involved in observing actions” taken by others (the hand on the screen) to grasp objects. The team is eager to figure out what function this dual activity serves.

—Jonathan Beard





SpongeBob vs. Batman

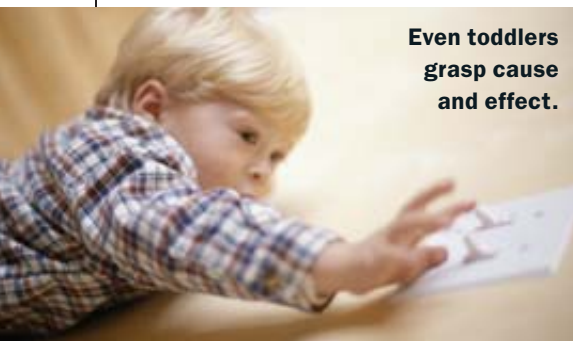
The ability to distinguish multiple fantasy worlds may be an innate skill. “Children’s meta-physical reasoning is much more complicated than previously thought,” says Deena Skolnick, a doctoral candidate in psychology at Yale University.

In a recent study entitled “What Does Batman Think about SpongeBob?” Skolnick and Yale psychology professor Paul Bloom asked 24 adults and 24 children ages four to six questions about familiar fictional characters. For example: Is Batman real? Does Batman think Robin is real? Does Batman think Nemo is real? (For those playing at home, the popular answers kids gave were no, yes, no.) In most cases, the youngsters’ responses closely matched the adults’. Notably, the kid crusaders did not simply place all make-believe characters in one universe.

To further test the claim that children make this multiworld distinction on their own, the dynamic duo now plans to test three-year-olds and also to explore how kids deal with their own pretend worlds. “Our hunch is that certain facts about how fiction works are not learned; they are natural by-products of the architecture of the human imagination,” Bloom explains. That would mean that the flight of fancy needed to write a novel or appreciate a blockbuster might spring from the same skills we use to predict what might be happening around a corner ahead of us or in an upcoming week. From the everyday to the extraordinary, we spend much of our lives immersed in hypothetical scenarios, and Skolnick hopes to track how we manage them all. The cartoon query, she says, “is just a first step.”

—Matthew Hutson

Preschool Determinists



Even toddlers grasp cause and effect.

Kids do not need school to learn about cause and effect; they believe in causal laws well before kindergarten.

When cognitive scientists Laura E. Schulz of the Massachusetts Institute of Technology and Jessica Sommerville of the University of Washington tested preschoolers, they discovered that the kids were thoroughgoing “causal determinists.” The children assumed that everything happens for a reason. Schulz and Sommerville showed the kids toy lights and switches that either worked all the time or only some of the time. The

children then were asked to make them light up—or to prevent them from lighting. “The children consistently behaved as if the lights and switches operated sensibly—that effects happened for reasons,” Schulz says. When the contraptions were rigged to shine only occasionally, “children looked for hidden switches that might have blocked the toys, rather than accepting that the toys might operate at random.”

The children’s fundamental assumptions both “enabled” and “constrained” their search for causes for the lights’ behavior, Schulz adds. For example, children proposed ideas about hidden switches to explain why a toy might not always work. The insights are important, Schulz explains, because children’s theoretical frameworks affect their learning processes. Sommerville says that knowing that children hunt for and observe causes can help teachers find more effective ways to transfer knowledge.

In future research Schulz wants to look at how children deal with “psychological indeterminacy”—when people do not always return a smile, for example. “They may use a different set of assumptions when they analyze human behavior,” she says. —Jonathan Beard

FAST

■ **Goth teens** say they are simply “different,” yet researchers at the University of Glasgow in Scotland have substantiated a severe dark side. They surveyed 1,258 young people at age 11 and again at 13, 15 and 19. Self-identification as a Goth was more strongly associated with self-harm (53 percent) and attempted suicide (47 percent) than any other youth subculture, including Punk and Mosher—and it was a stronger factor than social class, parental separation, smoking, alcohol use or previous depression.

■ **Overweight people** in their 40s have yet another reason to shed pounds: obesity elevates their risk of developing Alzheimer’s disease. Researchers at the Kaiser Permanente Foundation Research Institute in Oakland, Calif., charted nearly 9,000 people for up to 30 years beyond their 40s. The heavier people were, the more likely they were to develop dementia. Future studies are needed to examine the molecular mechanisms linking obesity and Alzheimer’s.

■ **Depressed** white girls are more likely to grow out of their funk than black girls are, according to a Northeastern University study of 2,221 females age 16 to 23. White teens become less depressed as they reach early adulthood, whereas the depression rate among blacks holds steady. Professors blame poorer health care, lack of insurance and stronger social stigma as main factors sustaining the malady for black women.

Neuro Nurses Unite

A patient recovering from a head injury in a neurological intensive care unit (ICU) might be surprised to learn that the nurses caring for him had little training in neuroscience beyond the typical four hours of lecture in nursing school. Some leading caregivers are trying to change that. Joanne V. Hickey, a neuroscience nurse scholar and clinical expert at the Methodist Neurological Institute in Houston, and Ann Quinn Todd, nursing director of the institute's Eddy Scurlock Stroke Center, joined forces to organize the institute's inaugural symposium on neurological nursing. More than 150 practitioners attended.

Neurological nursing focuses on treating injuries and diseases of the brain and nervous system, such as stroke, aneurysms and neurodegenerative conditions such as Parkinson's. The field has existed for 60 years but "has long played second fiddle to cardiovascular nursing," Todd says. "Heart has always been the biggest competition, but it's just a pump!" Recent times have brought innovations such as improved magnetic resonance imaging technology and instruments like the MERCI corkscrew, which nurses can insert to extract blood clots from the brains of patients who suffer embolic strokes. These tools and more were featured in hands-on exhibits at the symposium, which also offered seminars on the electronic ICU, pituitary tumors and brain stem cells.

"If the interest is there—and so far it is," Todd notes, the symposium will grow each year, introducing neurological nurses in Texas and across the country to the latest discoveries and techniques. Such local meetings could augment national efforts such as those of the American Association of Neuroscience Nurses.

—Kaspar Mossman



Training
would improve
nursing care
of head
injuries.

The Jilted Brain

Most of us know how terrible it feels to be in the throes of a breakup. Now scientists know what it looks like, too. Helen Fisher, an anthropologist at Rutgers University, and several neuroscience colleagues found some interesting correlations after scanning the brains of 10 women and five men who were still heartsick over losing a lover.

The investigators positioned each jilted subject in a functional magnetic resonance imaging scanner. When they asked the volunteers to look at a photograph of their former lover and at a neutral picture, they found that the same areas at play in new love—for example, the nucleus accumbens that governs reward—were still active when the forlorn looked at their lost love. But new areas were also activated, including those that regulate obsessive-compulsive thoughts and anger, suggesting a torrent of mixed emotions.

Stress regions also lit up strongly. "Being rejected in love is among the most painful experiences a human being can endure," Fisher says. She suspects that such brain reactions moderate over time, probably by biological design, perhaps to aid self-preservation. Yet if the individuals are lucky, they will meet someone new, and the biological processes will start all over again.

—Jamie Talan



GETTY IMAGES (top); D. ARKY Photex/zefa/Corbis (bottom)

Focusing on attractive features can ward off eating disorders.

Eye of the Beholder

The only factor separating someone from an eating disorder may be a healthy dollop of self-delusion.

Psychologists have tried to identify whether individuals with eating problems have distorted perceptions or feelings about their bodies, but the findings have been unconvincing. Researchers from the University of Maastricht in the Netherlands recently tried a different approach. First they asked individuals from two groups to rate their own attractiveness. One group had symptoms of eating disorders. People in the other, control group had been chosen because their (normal) body sizes were similar to those of the disordered group. The investigators presented pictures of everyone's bodies, with the heads cropped out, to two panels of evaluators. Somehow, despite the size similarity, both sets of evaluators rated those with eating disorders as less attractive—in accord with the ratings the disordered individuals gave themselves.

In contrast, the control subjects overestimated their own attractiveness, suggesting they have a biased, protective body image. To treat people with eating disorders, doctors might teach them to focus on their attractive features, the experimenters propose.

—JR Minkel



Better Than Individuals

When three, four or five people gather to solve a problem, chances are they will succeed beyond the efforts of an equivalent number of individuals working separately, even if those soloists are the brightest available. So conclude researchers at the University of Illinois.

The investigators enrolled 760 of the school's students to solve complex letter and word problems. Some toiled as individuals while others functioned in groups of two, three, four or five. The groups of three, four and five performed better than any set of individuals.

The dynamic is sensitive, however. Teams of two performed at the same level as two separate people, suggesting that this team size is too small to foster the dynamics that create optimal problem solving. Also interesting is that groups of three, four and five did equally well compared with one another; there was no advantage to adding people beyond a trio.

Study leader Patrick R. Laughlin says that in addition to tackling workplace challenges, problem-solving groups might enhance classroom learning. Further research is needed to determine whether student groups perform better than individuals do in academic settings and, if so, at what ages and tasks.

—Mark Fischetti



Age at Work

Older workers are not necessarily slower than younger workers, and often they make fewer errors
BY MICHAEL FALKENSTEIN AND SASCHA SOMMER

THEY MOVE TOO SLOWLY, forget things and are inflexible. They don't do teamwork and can't adapt to new technologies. Many people describe older workers in these terms, and the characterizations are often the reasons personnel managers give for hiring younger employees instead.

But are these views substantiated? Do older employees in fact perform poorly? If so, at what tasks? Neuroscientists and psychologists active in the field of "cognitive gerontology" are investigating these questions. What they have found so far is surprising: although older people may be slower at some tasks, they are actually faster at others, and in most cases they are less prone to mistakes. The research also reveals that only certain brain functions are affected by possible age-related deficits and that simple changes in the workplace can compensate for them.

Faster May Not Be Better

There is great emphasis in today's work environment on speed and flexibility. Even delivery drivers, who for years followed the same routes, now find that their courses may change daily. Handling a changing environment requires "fluid intelligence"—the ability to switch readily between different tasks, redirect attention, and block out irrelevant or distracting information.

Older people do tend to find it difficult to coordinate competing tasks, as psychologist Jutta Kray of Saarland University in Germany has shown. She presented subjects of various ages with images on a computer screen and asked questions that forced subjects to switch quickly between identifying



particular shapes and colors on changing displays. Participants older than 50, on average, did not do as well. For them, the mental effort required for task switching was greater.

But there was good news, too, which put the image of the "inflexible old" into perspective. The older subjects did considerably better after they rehearsed ways to improve their responses. Their success indicates that age-related performance deficits can be overcome if work situations are constructed in the appropriate way.

As research improves, many examples of supposed age-related deficits will dissolve. We recently collaborated with Juliana Yordanova and Vasil Kolev of the Bulgarian Academy of Sciences in Sofia on experiments that painted a finer picture of mental functions.

In one test, we presented volunteers of various ages with four letters: A, E, I, O. They saw the letters appear randomly on a screen, one after another, or heard them being pronounced through headphones. We asked the subjects to respond to each letter as quickly as

Contrary to **common wisdom**, tests show that older people are not more susceptible to distraction.

GETTY IMAGES

possible by pressing a button, but they had to use a different finger for each letter. This so-called choice reaction task thus forced them to decide anew each time how to react. Other subjects, acting as controls, were told to respond using the same single finger in every case.

We used electroencephalograms to measure the event-related potentials—the brain waves that arose during sensory perception and cognitive processing. By examining the components of these waves, we can follow individual neuronal processes. For our reaction task, the first part of the

actual motor response might be slightly slower, that can be an advantage: a low error rate is exactly what employers value in quality-control jobs.

Distraction!

Other experiments we conducted revealed that older people make fewer mistakes largely because they are less easily distracted. This finding was surprising, because common wisdom says older people are more susceptible to distraction.

Visual distraction tests, done on a computer screen by our group and

Restructuring Offices and Brains

Because older people perform even better than the young on many tasks, it is wrong to categorize them as generally less capable. And modest deficits can be overcome by adjusting the work environment. With neurophysiological testing, researchers can pinpoint the causes of lackluster performance and redesign workplaces appropriately.

We should also note that in the real business world, speed and accuracy are not the only success factors. Older employees typically have gained knowledge with experience that younger em-

(Any modest **performance deficits** can be overcome by redesigning the workplace environment appropriately.)

signal represented the processing of the visual or auditory stimuli, the second related to the thinking and decision making involved, and the third corresponded to the brain signal that prepares a finger to move.

As expected, the older subjects took somewhat longer, and yet they made fewer mistakes (using the wrong finger). The reason was interesting. Detailed analysis showed that older people processed visual and auditory stimuli just as quickly as younger people did. Their brains also thought and made decisions just as well. The only lag occurred during the final phase—the brain signal that prepares the finger to move. In older subjects the threshold to initiate a motor response was higher. Older brains seemed to operate according to the motto: “Better to be slow but right.” Numerous other event-related-potential studies have reached the same conclusion.

This insight has important implications for the workplace. Certain jobs demand frequent choices and categorization—for example, the quality-control function at a manufacturing company. Because studies show that these processes are not significantly affected in older workers, there is no reason to deny them such jobs. And although the

Bruno Kopp, a neuropsychologist at the University of Braunschweig in Germany, also showed the value of delayed response. Essentially, when distracting lights appeared on a screen, younger participants initiated the action to (wrongly) push a button before they fully comprehended that their reaction would be incorrect. Older people began their “push the button” activation signal later, which prevented them from making mistakes. The subjects who were slower had an immense performance advantage. This ability can be very useful in numerous jobs, not to mention in daily life situations such as guiding a car through a busy, distraction-filled intersection.

Our studies do show that seniors do not perform as well under severe time pressure, especially if they must visually search for a target. In this circumstance, older subjects had both longer reaction times and higher error rates. They also found the test more stressful. But here, too, such problems could be mitigated in the workplace. Older truck drivers, for example, could be given onboard navigation systems that provide spoken directions instead of a map on a small display. Indeed, our group is now studying how such a system ought to be designed.

ployees do not have. In addition, older people often are more socially competent, making them attractive for customer contact and advising tasks.

Furthermore, even when an older employee might prove initially slower at a particular mental function, neural networks can restructure themselves over time. For example, cognitive neuroscience professor Roberto Cabeza of Duke University has shown that seniors who performed poorly on a memory test activated the same brain regions as young subjects, yet seniors who did well had a different activation pattern. These results make it clear that neuronal restructuring can help compensate for deficits—although not every older brain is capable of carrying that out.

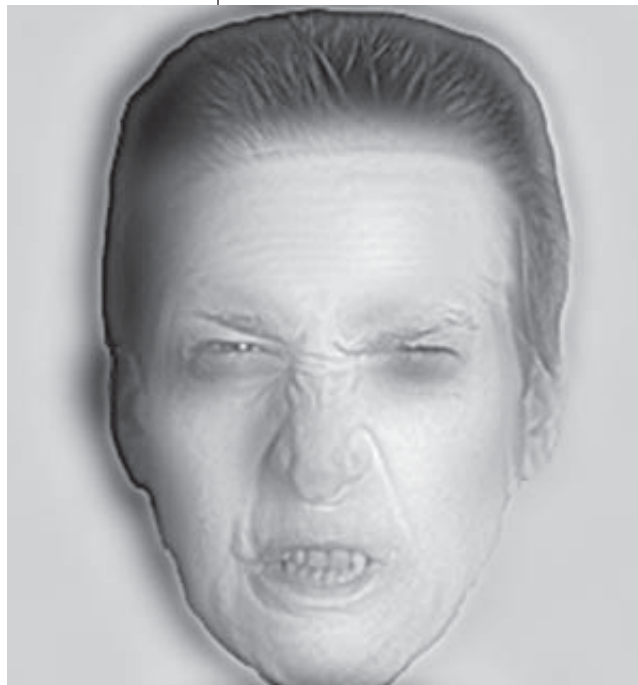
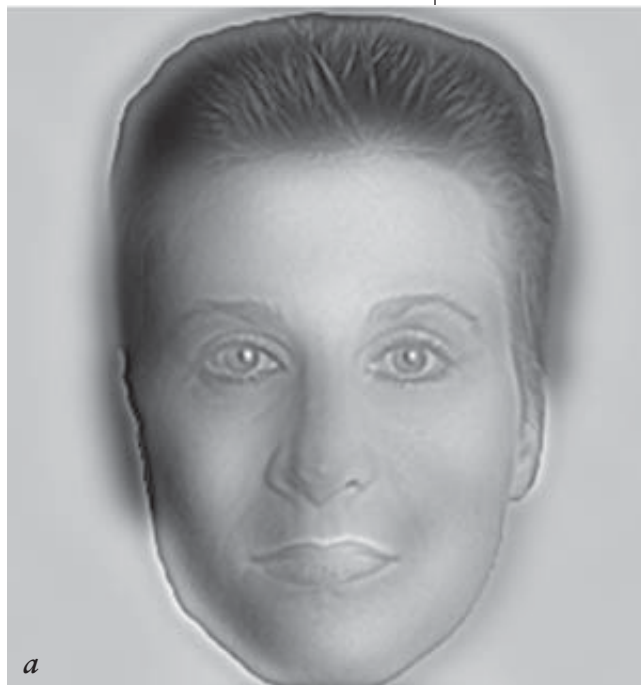
Restructuring workplaces and brain networks will both be necessary in tomorrow’s labor market. Retirement ages are rising. Low birth rates mean fewer people will enter the workforce. Personnel offices that equate “over 45” with “too old” may be overlooking a major source of needed employees. **M**

MICHAEL FALKENSTEIN leads the Age and Central Nervous System Changes Project at the University of Dortmund’s Institute for Occupational Physiology in Germany. SASCHA SOMMER is a researcher there.

Cracking the Da Vinci Code

What do the *Mona Lisa* and President Abraham Lincoln have in common?

BY VILAYANUR S. RAMACHANDRAN AND DIANE ROGERS-RAMACHANDRAN



SPANISH PAINTER EL GRECO often depicted elongated human figures and objects in his work. Some art historians have suggested that he might have been astigmatic—that is, his eyes' corneas or lenses may have been more curved horizontally than vertically, causing the image on the retina at the back of the eye to be stretched vertically. But surely this idea is absurd. If it were true, then we should all be drawing the world upside down, because the retinal image is upside down! (The lens flips the incoming image, and the brain interprets the image on the retina as being right-side up.) The fallacy arises from the flawed reasoning that we literally “see” a picture on the retina, as if we were scanning it with some inner eye.

No such inner eye exists. We need to think, instead, of innumerable visual mechanisms that extract information from the image in parallel and process it stage by stage, before their activity culminates in perceptual experience. As always, we will use some striking illusions to help illuminate the workings of the brain in this processing.

Angry and Calm

Compare the two faces shown in *a*. If you hold the page about nine to 12 inches away, you will see that the face on the right is frowning and the one on the left has a placid expression.

But if you move the figure, so that it is about six or eight feet away, the expressions change. The left one now smiles, and the right one looks calm.

How is this switch possible? It seems almost magical. To help you understand it, we need to explain how the images were constructed by Philippe G. Schyns of the University of Glasgow and Aude Oliva of the Massachusetts Institute of Technology.

A normal portrait (photographic or painted) contains variations in what neuroscientists such as ourselves term “spatial frequency.” We will discuss two types of spatial frequency: The first is “high”—with sharp, fine lines or details present in the picture. The second is “low”—conveyed by blurred edges or large objects. (In fact, most images contain a spectrum of frequencies ranging from high to low, in varying ratios and contrasts, but that is not important for the purposes of this column.)

Up close, one face frowns and the other looks calm.
Viewed from farther away, **the two faces change**. How?

(Squint, and the image blurs, eliminating the sharp edges.
Presto! Lincoln becomes instantly recognizable.)

Using computer algorithms, we can process a normal portrait to remove either high or low spatial frequencies. For instance, if we remove high frequencies, we get a blurred image that is said to contain “low spatial frequencies in the Fourier space.” (This mathematical description need not concern us further here.) In other words, this procedure of blurring is called low-pass filtering, because it filters out the high spatial frequencies (sharp edges or fine lines) and lets through only low frequencies. High-pass filtering, the opposite procedure, retains sharp edges and outlines but removes large-scale variations. The result looks a bit like an outline drawing without shading.

These types of computer-processed images are combined together, in an atypical manner, to create the mysterious faces shown in *a*. The researchers began with normal photographs of three faces: one calm, one angry and one smiling. They filtered each face to obtain both high-pass (containing sharp, fine lines) and low-pass (blurred, so as to capture large-scale luminance variations) images. They then combined the high-pass calm face with the low-pass smiling face to obtain the left image. For the right image, they overlaid the high-pass frowning face with the low-pass calm face.

What happens when the figures are viewed close-up? And why do the expressions change when you move the page away? To answer these questions, we need to tell you two more things about visual processing. First, the image needs to be close for you to see the sharp features. Second, sharp features,

when visible, “mask”—or deflect attention away from—the large-scale objects (low spatial frequencies).

So when you bring the picture near, the sharp features become more visible, masking the coarse features. As a result, the face on the right looks like it is frowning and the one on the left, like it is relaxed. You simply do not notice the opposite emotions that the low spatial frequencies convey. Then, when you move the page farther away, your visual system is no longer able to resolve the fine details. So the expression conveyed by these fine features disappears, and the expression conveyed by low frequencies is unmasked and perceived.

The experiment shows vividly an idea originally postulated by Fergus Campbell and John Robson of the University of Cambridge: information

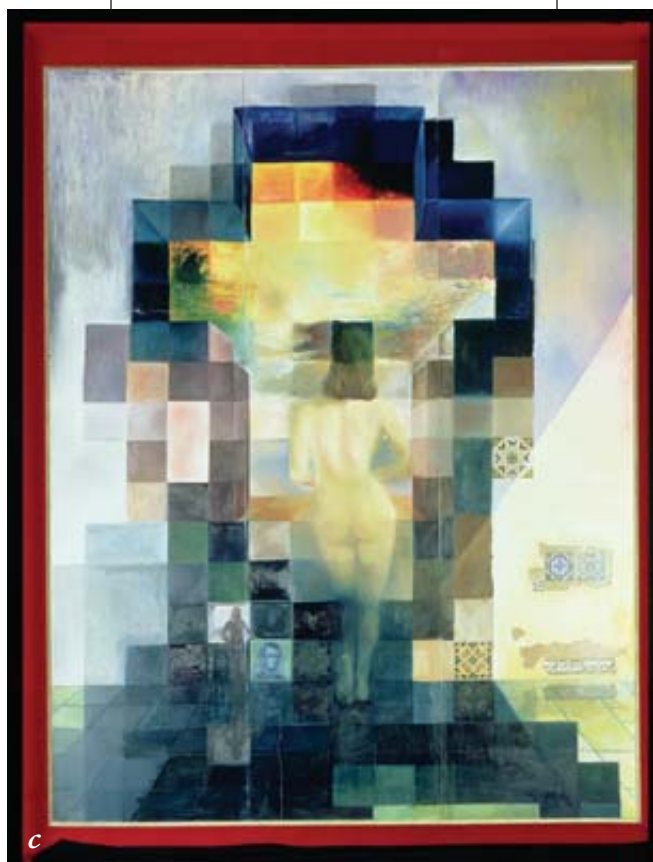


from different spatial scales is extracted in parallel by various neural channels, which have wide ranges of receptive field sizes. (The receptive field of a visual neuron is the part of the visual field and corresponding tiny patch of retina to which a stimulus needs to be presented to activate it.) It also shows that the channels do not work in isolation

from one another. Rather they interact in interesting ways (for example, the sharp edges picked up by small receptive fields mask the blurred large-scale variations signaled by large receptive fields).

Honest Abe

Experiments of this kind go back to the early 1960s, when Leon Harmon, then working at Bell Laboratories, devised the famous Abraham Lincoln effect. Harmon produced the picture of Honest Abe (*b*) by taking a regular picture and digitizing it into coarse pixels (picture elements). Even when viewed close-up, there is enough information in the blocky brightness variations to recognize Lincoln. But these data, as we noted already, are masked by the sharp edges of the pixels. When you move far away from the



(The **elusive smile** can be seen only when you look away from the mouth. Attend to it out of the corner of your eye.)



photograph or squint, the image blurs, eliminating the sharp edges. Presto! Lincoln becomes instantly recognizable. The great artist Salvador Dalí was sufficiently inspired by this illusion to use it as a basis for his paintings, an unusual juxtaposition of art and science (c).

Mysterious *Mona Lisa*

Finally, consider the mysterious smile of Leonardo da Vinci's *Mona Lisa*. Philosophers and art historians who specialize in aesthetics often refer to her expression as “enigmatic” or “elusive,” mainly because they do not understand it. Indeed, we wonder whether they prefer not to understand it, because they seem to resent any attempts to explain it scientifically, apparently for fear that such analysis might detract from its beauty.

But recently neurobiologist Margaret Livingstone of Harvard Medical School made an intriguing observation; she cracked the da Vinci code, you might say. She noticed that when she looked directly at Mona Lisa's mouth (d, center panel), the smile was not apparent (quite a disappointment). Yet as she moved her gaze away

from the mouth, the smile appeared, beckoning her eyes back. Looking again at the mouth, she saw that the smile disappeared again. In fact, she noted, the elusive smile can be seen only when you look away from the mouth. You have to attend to it out of the corner of your eye, rather than fixating on it directly. Because of the unique shading (placement of low spatial frequencies) at the corners of the mouth, a smile is perceived only when the low spatial frequencies are dominant—that is, when you look indirectly at the masterpiece.

To confirm this notion, she performed a low-pass filtering (left panel) and a high-pass filtering (right panel) of the *Mona Lisa*. Notice that with the low-pass (blurred) image the smile is more obvious than in the original—it can be seen even if you look directly at the mouth. With the high-pass (outlinelike) image, however, no smile is apparent, even if you look away from the mouth. Putting these two images

back together restores the original masterpiece and the elusive nature of the smile. As with the changing faces, we can now better appreciate what Leonardo seems to have stumbled on and fallen in love with—a portrait that seems alive because its fleeting expression (thanks to quirks of our visual system) perpetually tantalizes the viewer.

Taken collectively, these experiments show that there is more to perception than what meets the eye. More specifically, they demonstrate that information at different scales, such as fine versus coarse, may be extracted initially from an image by separate neural channels and recombined at different stages of processing to create the final impression of a single unified picture in your mind. **M**

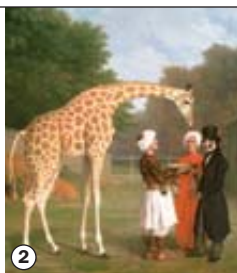
VILAYANUR S. RAMACHANDRAN and DIANE ROGERS-RAMACHANDRAN are at the Center for Brain and Cognition at the University of California, San Diego.

(Further Reading)

- ◆ **Dr. Angry and Mr. Smile: When Categorization Flexibly Modifies the Perception of Faces in Rapid Visual Presentations.** Philippe G. Schyns and Aude Oliva in *Cognition*, Vol. 69, No. 3, pages 243–265; 1999.



1



2



3



4



5

MUSEUMS/EXHIBITIONS

1 The Cult of Saints

From the Middle Ages to today, religious devotion to saints has had a profound impact on the culture of Europe and its intellectual descendants. The Getty looks back and around at this cult "through images created in its service."

Getty Center, Los Angeles

April 25–July 16

www.getty.edu/

Snapshot Chronicles: Inventing the American Photo Album

Snapshots became the visual cornerstone of countless personal narratives after the Kodak Brownie went on sale in 1900. This exhibition focuses on ordinary lives during extraordinary events: the story of San Franciscans who recorded their experience during and after the great earthquake of 1906.

San Francisco Public Library,

Jewett Gallery

April 8–August 20

415-557-4277

www.sfppl.org/

2 Fierce Friends: Artists & Animals, 1750 to 1900

Influenced by the social changes wrought by the industrial revolution and the ideas of Darwin, attitudes about the natural world changed profoundly during the 18th and 19th centuries. This exhibition, co-organized by the Carnegie Museum of Art and the Van Gogh Museum in Amsterdam, looks at how artists portrayed "humanity's relationship with nature as exemplified through our treatment of animals."

Carnegie Museum of Art, Pittsburgh

March 25–August 27

412-622-3131

www.cmoa.org/exhibitions/exhibit.asp

CONFERENCES

Neuro-Psychoanalytic Society

"Love and Lust in Attachment" is the theme. The goal is finding ways for neuroscience to inform psychoanalytic thinking on these matters. Speakers include an-

thropologist Helen Fisher, author of *Why We Love* (Henry Holt, 2004), and Jaak Panksepp, a neuroscientist at Bowling Green University who has studied social attachment since the 1970s.

Pasadena, Calif.

July 21–23

44-20-7443-9344

www.neuro-psa.org

3 American Psychoanalytic Association

Bonnie E. Litowitz, a psychiatrist at Rush University Medical Center, will give a lecture on "The Second Person."

June 16–18

Washington, D.C.

212-752-0450

www.apsa-conference.org/

MOVIES

The Break-Up

Love versus affordable housing: an emotional donnybrook ensues when Brooke (Jennifer Aniston) and Gary (Vince Vaughn) quit their relationship but are both unwilling to quit the premises of their condo. This comedy descends to darker realms of nastiness as each side tries to drive out the other. Despite the un-*Friends*-liness, there are rumors of a happy resolution.

Universal Pictures

In wide release

www.thebreakupmovie.net/

Wordplay

Fans of our Head Games, as well as the 50 million Americans who enjoy racking their brains doing crossword puzzles every week, will appreciate this documentary on the *New York Times*/NPR puzzle guru Will Shortz. There are also interviews with puzzle fans such as Bill Clinton and Bob Dole.

Distributed by IFC Films

In wide release

www.wordplaythemovie.com/

4 A Scanner Darkly

An animated version of Philip K. Dick's novel about police fighting the war on the fictional drug "Substance D." Those addicted

to it develop Jekyll-and-Hyde-like split personalities: the narcotics cop Fred (Keanu Reeves) is at odds with his Hyde self, Bob the drug dealer.

Warner Independent Pictures

Opens July 7

<http://wip.warnerbros.com/index.html?site=ascannerdarkly>

World Trade Center

Apparently Hollywood thinks enough time has passed since the death and destruction of September 11, 2001, to start making movies with a feel-good twist. This one is based on the real-life stories of two lucky people who survived the attack, John McLoughlin (Nicolas Cage) and William Jimeno (Michael Peña). In the hands of director Oliver Stone, the film may reawaken old fears, or it may provide a catharsis for the country. Or maybe nobody will see it. It's not exactly a date movie.

Paramount Pictures

Opens August 11

www.wtcmovie.com/

WEB SITES

<http://serendip.brynmawr.edu/>

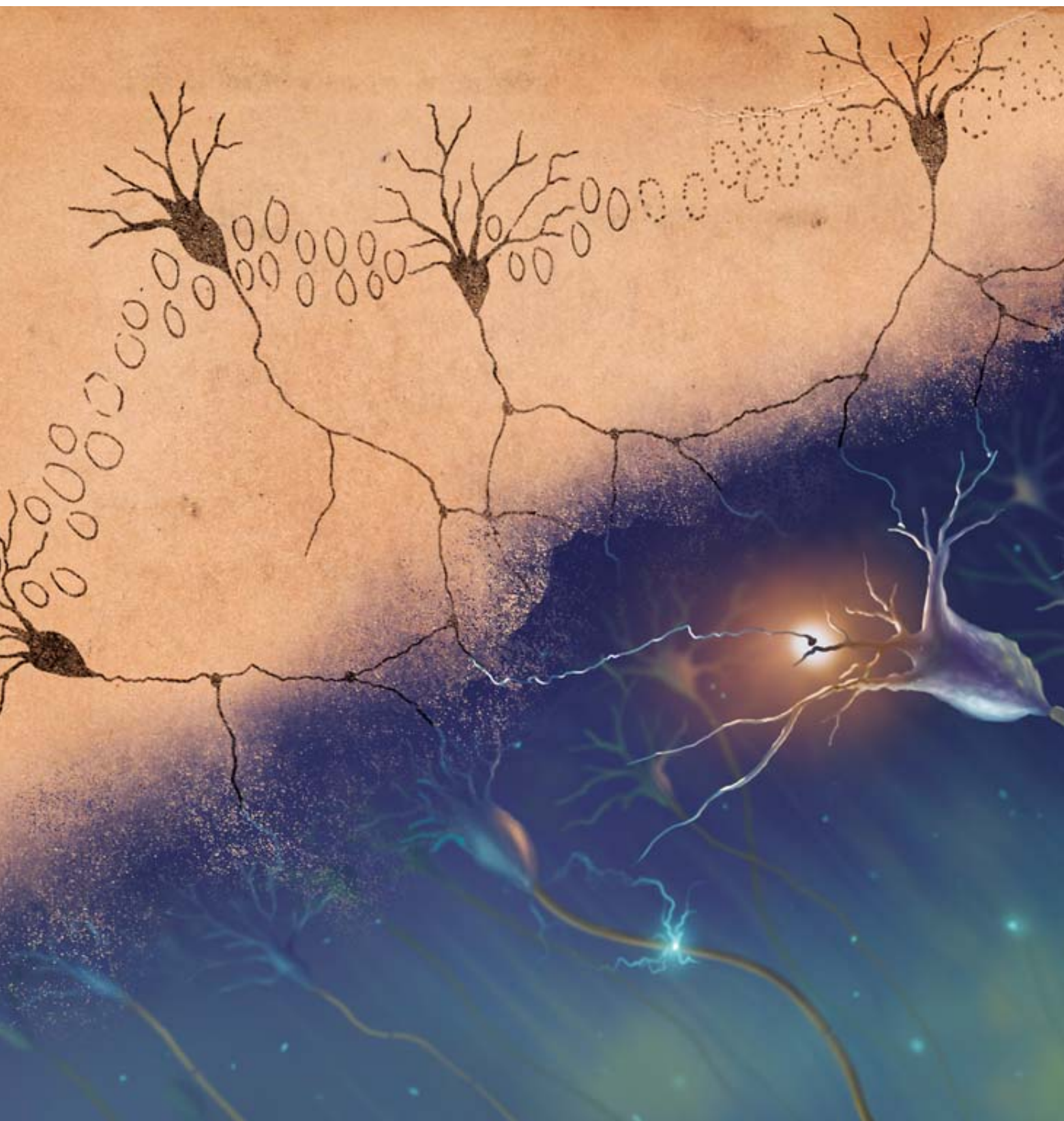
Serendip, hosted by Bryn Mawr College, is "a gathering place for people who suspect that life's instructions are always ambiguous and incomplete." The site is as extensive as the definition is broad, bringing you readings, musings, interactive exhibits and "germinal zones" within such fields as "Brain and Behavior" and "Science and Culture." Current guest exhibits include "Mind and Body: René Descartes to William James."

5 <http://web.mit.edu/museum/exhibitions/robots.html>

If you can't get to the Massachusetts Institute of Technology Museum in Cambridge, Mass., you can visit "Robots and Beyond: Exploring Artificial Intelligence @ MIT." Get acquainted with Cog and Kismet, two pioneers from the frontier of machine intelligence.

Send items to editors@sciammind.com

COURTESY OF J. PAUL GETTY MUSEUM (1); JACQUES-LAURENT AGASSE, THE NUBIAN GIRAFFE, Carnegie Museum of Art, The Royal Collection, Her Majesty Queen Elizabeth II (2); COURTESY OF BONNIE E. LITOWITZ (3); © 2005 WARNER BROS. ENTERTAINMENT (4); COURTESY OF THE MIT MUSEUM (5)



Beyond the Neuron Doctrine

New experiments are settling a century-long debate between two camps over how neurons communicate. **The surprise: both sides are right**

I sliced the heart in two with a big kitchen knife. All was revealed—the four chambers separated by moist, gristly valves that suck blood into auricles and squeeze it out ventricles. Eleven years old and fascinated, I asked my mother if, next time, she could bring me a brain. When she returned from the butcher shop with a calf brain, I beamed and cleaved the melon in two. But inside I saw nothing notable. Just a hollow cavity at the core of a fleshy mush.

How did it work? Books offered names for its bumps and folds but failed to provide a detailed explanation for how this supreme organ functioned. My parents, teachers—no one seemed to have the answer.

Today we know the brain's power comes from components so miniaturized they are invisible. But even though technology now allows us to see individual neurons, our models of how they function en masse are still inadequate. We like to think of each cell as a microprocessor linked to billions of others. But how sure can we be that this analogy is accurate? Are we held captive by our analogies just as tightly as the scientists who preceded us were bound by their own now obsolete ideas?

By R. Douglas Fields

DON BLISS/NIH Medical Arts, REPRINTED WITH PERMISSION FROM T. H. BULLOCK ET AL. IN SCIENCE, VOL. 310, NOVEMBER 4, 2005. © AAAS



Camillo Golgi



Santiago Ramón y Cajal

The answer is yes. The discoveries are convincing neuroscientists that our fundamental concept of how the brain works is naive. Yet ironically, the two prevailing models, which have been at odds since their founders were jointly awarded the Nobel Prize 100 years ago, are both relevant. Indeed, by joining the models and adding a third, yet unanswered piece to the puzzle raised by recent research—how brain cells give rise to brain waves—we can finally explain not only how the human brain works but also what makes it unique in the animal world.

Networked or Isolated

Analogies are helpful because they make complicated situations more accessible. But such simplification also encourages rigid thinking. As the 20th century approached, anatomists probed the brain with the most powerful instrument available: the newly perfected microscope. They peered into an invisible world of baffling complexity, a densely tangled mass of microscopic, interconnected fibers. Anatomists naturally presumed that these tiny tubes, called axons, were like pipes, plumbed into a Byzantine network that allowed sensations and commands to flow freely to wherever they were required. The neuron was simply a node in the interconnected network.

One man looking at this world saw something different, however. The great Spanish anatomist Santiago Ramón y Cajal was at heart an artist. As a boy, he sketched cadavers dissected by his physician father before he, too, became a doctor. With an artist's ability to see motion in the curve of a line, Ramón y Cajal began to see a logic in the tangle of cells and pipes. His vision, hotly contested for the next 50 years, became known as the neuron doctrine.

Ramón y Cajal observed that a single, long axon running from one neuron tended to end in a field of dendrites—other, short tubes attached to another neuron. He maintained, however, that the tubes were not interconnected everywhere. In a brilliant deduction, Ramón y Cajal concluded that each neuron was an island unto itself, not a node in a network. Moreover, he surmised that information flowed in one direction: into dendrites, then through a neuron cell body, and out its axon.

Furthermore, the axon did not connect with the dendrites. It remained separated by a minuscule gap, or synapse. This gap functioned as a switch that allowed information to pass to the next neuron—or not. The space of separation was so small it was beyond the resolution of the best microscopes. Scientists would not get their

PHOTO RESEARCHERS, INC. (left); THE NOBEL FOUNDATION (right)

first fuzzy glimpse of the synapse until the 1950s, when focused electron beams replaced light beams in microscopes.

In 1906 the Nobel Prize in Physiology or Medicine was awarded jointly to Ramón y Cajal and his rival, Italian physician Camillo Golgi. The unusual pairing sparked a standoff in modeling how the brain works that is only being settled today, on the award's centennial. Like many others, Golgi assailed the validity of the neuron doctrine and vigorously defended the free-flowing network view of the brain. The great irony was that Ramón y Cajal used an ingenious lab technique Golgi had invented to provide evidence

connection appeared to be direct and electrical.

When the electron microscope finally revealed the synapse in 1955, scientists again were faced with evidence for both sides. There was no longer any doubt that neurons were stand-alone entities or that they communicated across the gap using chemical messengers. But some images showed individual neurons to be connected to one another, as though spot-welded. Researchers soon determined that protein channels, called gap junctions, formed these welds—like a short coupling that joins two hoses. Ions and organic molecules passed freely, allowing impulses to speed directly from one neuron to the next.

(Neurons can **release neurotransmitters** far away from synapses, an overlooked form of communication.)

for his neuron doctrine. Golgi had devised a way to stain nerve cells with silver nitrate, making their features visible against background tissue. For reasons that are still not understood, the Golgi method stains only a fraction of neurons in a sample, but the neurons that absorb the stain are revealed in exquisite detail. Ramón y Cajal's pen-and-ink drawings of Golgi-stained neurons were the basis of his theory. Golgi was backed into the uncomfortable predicament of arguing that his marvelous Nobel Prize-winning procedure was merely producing an artifact when it showed neurons as individual cells.

Welded Together

The debate between doctrinaires who supported Ramón y Cajal's neuron doctrine and reticularists (from the Latin for "network") who supported Golgi's scheme raged for decades because every new tool turned up evidence fueling both arguments. For example, electrophysiologists, using electrodes and electronic amplifiers to study the transmission of electrical signals from axon to dendrite, proved in fine detail that when an impulse reached the end of an axon, the axon released chemical substances called neurotransmitters. This event was followed by a delay of about $1/1,000$ of a second, as the substances diffused across the tiny synapse and stimulated an electrical response in the neighboring dendrite. Yet in some cases, the recordings showed that an electrical signal swept from axon to dendrite with no delay at all, as if the two nerve cells were fused. No neurotransmitters were involved, and the

Transmission of signals across "chemical" synapses—the basis for learning and memory—could be regulated by the release or uptake of neurotransmitters, so they drew most of the attention from neuroscientists. In contrast, "electrical" synapses appeared static, and their role in brain function was much less interesting. Electrical synapses seemed peculiar, relevant only when very rapid communication was necessary or when a bunch of neurons needed to be tethered to a group.

Yet recent work by neuroscientist Michael V. L. Bennett of Albert Einstein College of Medicine and others shows that simple view to be wrong: conduction through gap junctions can be regulated by changes in the voltage of cell membranes and by biochemical reactions that control the size of the channel through the junction. There are even cases where chemical and electrical synapses form together at the same junction. One thing is certain: Golgi was right. Neurons can be networked together.

A Changing Tide

Whether signals travel one way down a chain of neurons or back and forth across a network, using chemical or electrical messengers, even more fundamental questions remain: What do the signals mean? How do traveling impulses translate into a visual image, a feeling, a thought? What's the code? Neither model has provided answers, yet proponents have generated surprising insights that undermine the exclusivity of each theory.

One of the great discoveries made in examining the neuron doctrine is that neural impulses (called action potentials) carry information in one direction, from the cell body to the axon tip. Every morsel we taste, every idea we have, is described by a pattern of impulses firing through axons. Neuroscientists were eager to decipher this code, and they did. They found that the codebook changes constantly depending on the

firmed that many such neurons did not emit sharp, spiked impulses at all.

These small, tightly packed “interneurons” process information within internal circuits of the brain, rather than communicating directly with the body or environment as motor and sensory neurons do. Interneurons are concerned with the fundamental, internal workings of the brain rather than with transmitting commands

(Glia broadcast signals across hardwired neurons, coupling them together into functional groups.)

prior history of stimulation. The same frequency of impulses might signify very bright light when we are outside during the day and relatively dim light when we are inside at night. That is because the impulse code is concerned with reporting *changes* of state, rather than slavishly transcribing our every sensation. This phenomenon explains why when you pop your head through a fresh cotton T-shirt in the morning, you are flooded with sensations about the soft fabric, but soon afterward you are not aware of feeling the cloth at all.

Action potential coding explains a great deal, but it only goes so far. The same rules for impulses are used by animals down to the lowly earthworm. There must be more. American Theodore H. Bullock, one of the grand men of 20th-century neuroscience, fleshed out the code more than any other individual. The electrophysiologist and comparative neuroanatomist was interested in how information is coded in the nervous system in all types of animals, from snails to whales. He traveled from the Amazon rain forest to tidal pools everywhere with his electrodes and microscope. In 1959 Bullock published a paper in *Science* stating that in addition to high-speed nerve impulses firing through axons, many other electrical events were playing out in the background, deviating from the neuron doctrine. In particular, he observed slow surges and wanes in the voltage on nerve cell membranes. These potentials strongly influenced how many impulses an axon would fire in a burst and the probability that an axon would fire at all.

Moreover, a sharp impulse was needed only to transmit information over long distances. The slow voltage waves could easily spread in all directions across small, closely spaced neurons, and Bullock’s electrophysiological records con-

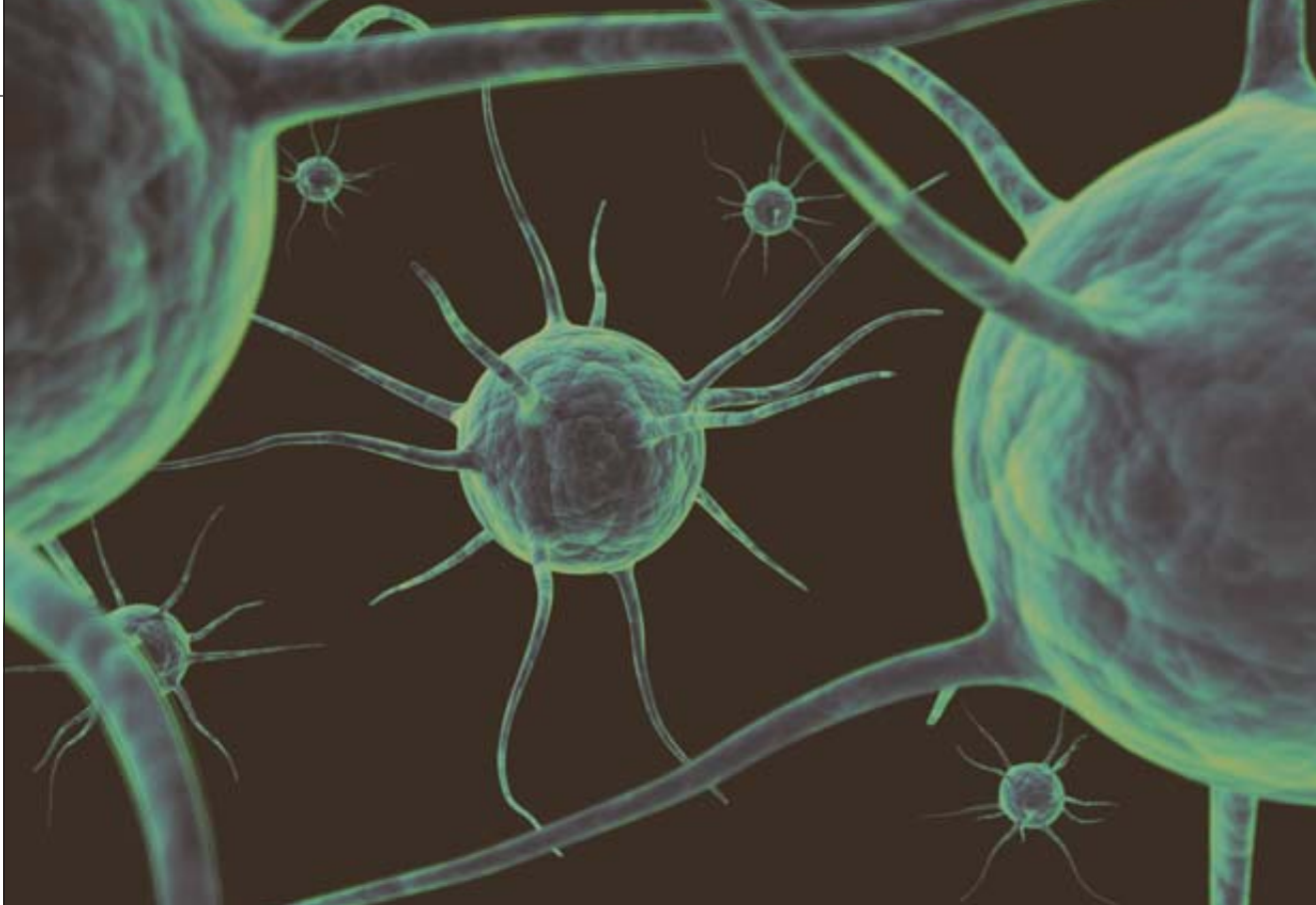
or sensations, and the neuron doctrine did not fit well for many of these internal processors. Roughly 100 billion interneurons in the human brain control information processing in learning and memory and are implicated in diseases such as epilepsy and Parkinson’s.

Leaks and Backflow

As Bullock further defined the workings of interneurons, other researchers exposed additional shortcomings of the neuron doctrine. Neuroscientist Daniel Johnston of the University of Texas at Austin inserted microelectrodes inside dendrites in the rat hippocampus and found two events that would have surprised Ramón y Cajal. In some circumstances, action potentials traveled not only down the axon but also “backward” into the cell body and down the dendrites. Moreover, dendrites did not simply collect incoming signals; in some instances, they fired impulses of their own. We now know it is likely that dendritic processing is part of the mechanism for learning and memory. Dendrites are more than passive conductors; they integrate and transmit information.

A recent surprise is that dendrites can also release hormones and peptides that influence the slow voltage changes on neuronal membranes, which affect whether a neuron fires a single impulse or bursts of impulses. Eve Marder of Brandeis University has found that these neuromodulators work when applied to axons, the neuron cell body, or dendrites, scrambling the orderly one-way information flow Ramón y Cajal perceived. Neuromodulators can even cause neurons to fire in rhythmic burst patterns; this firing forces ensembles of neurons to work in synchrony, like musicians playing in tempo.

Even the synapse proved less simple to under-



stand than originally suspected. Synapses did not form just between an axon and surrounding dendrites. Refined electron microscopes showed that synapses often appeared on the cell body of a neuron, on its dendrites, and from axon to axon and dendrite to dendrite. Neurons, it seemed, might indeed be connected in multidirectional networks much the way Golgi and the reticularists had imagined.

What is more, molecular neurobiologist Craig Jahr of the Vollum Institute at the Oregon Health & Science University recently proved that fast transmission using neurotransmitters can occur without any need for a synapse. At first, Jahr presumed that the neurotransmitters had seeped out of a nearby synapse, but his measurements indicated that neurons released the neurotransmitters through their cell membranes, far away from synapses. In 2005 computational neuroscientist Terrence J. Sejnowski of the Salk Institute for Biological Studies in La Jolla, Calif., and electron microscopist Mark H. Ellisman of the University of California, San Diego, concluded that this “ectopic” release of neurotransmitters outside synapses was an important and overlooked means of communication. If a neuron releases a single packet of neurotransmitters anywhere from its membrane, an adjacent neuron can detect it if it has neurotransmitter receptors in the vicinity. Today’s best electron microscopes show neurons

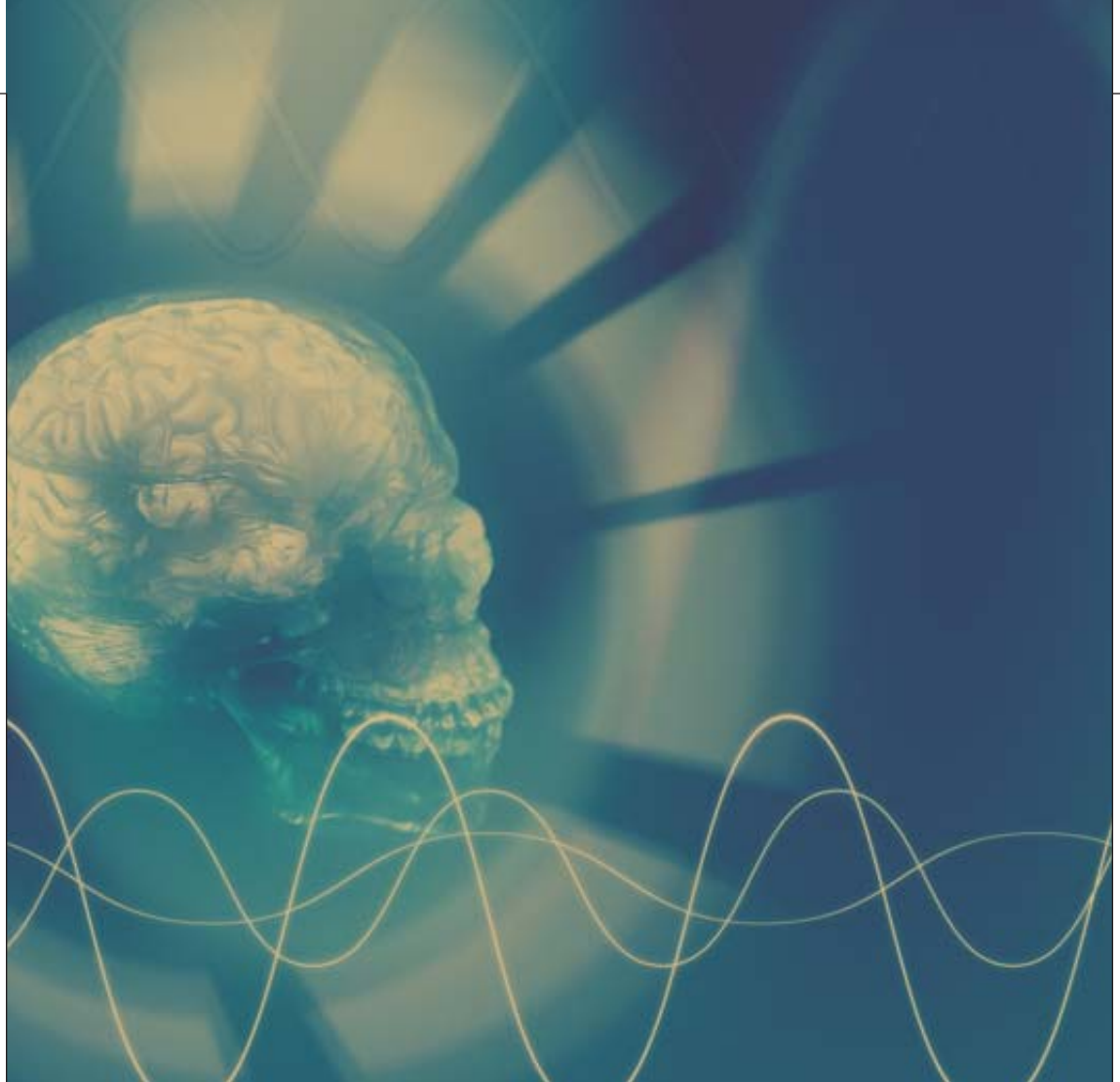
with thousands of these packets throughout their cell bodies. Suddenly, the model of how the brain processes information has become much more complicated.

The Glia Factor

Neuroscientists may be more willing to accept such heresy because of a startling expansion in thinking beyond the neuron doctrine in the early 1990s: most of the cells in the human brain are not neurons. Nearly 10 times as many cells, called glia, fill the space between neurons, and the ratio of glia to neurons increases in animals “higher” on the evolutionary tree. The very label “neuron doctrine” implies that neither Golgi nor Ramón y Cajal imagined that these cells had any information-processing function. For most of the 20th century, scientists believed glia provided only physical and nutritional support for neurons. But closer examination during the past decade has shown that glia have been listening in on conversations among neurons all along. Also astonishing has been the discovery that glia can communicate

(The Author)

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among themselves using chemical signaling (and no synapses are involved).

In addition, as glia eavesdrop they can control the flow of information among neurons. They perform this function by releasing or absorbing neurotransmitters or by controlling the concentration of ions surrounding neurons. Glia can also make and break connections between individual neurons.

Glia's habits violate the neuron doctrine in two ways. First, information flows through cells in the brain that are not neurons. Second, unlike neurons, which communicate through a series of links akin to telephone wires, glia communicate by broadcasting signals, the way cell phones do. Glia make shapeless connections that flow across the hardwired connections among neurons. In this way, glia can couple neurons together into functional groups. They communicate much more slowly than neurons do, but the speed may be adequate for many cognitive processes that do not require lightning-quick messages, such as the mechanisms that regulate mood and behavior.

To the neuron doctrine we now must add the glia doctrine: glia are equal partners in information processing. Glia intervene not only at synapses but also along axons by sensing impulses flowing through them. When axons fire bursts of action potentials, they release adenosine triphosphate (ATP) molecules, which are detected by receptors on all four types of glia. This information turns on and off genes in glia, affecting how they form layers of insulation around axons, which in turn affects how fast axons can conduct impulses. All of this communication moves along without synapses—a completely different channel of information flow in the brain.

Beyond Doctrine

Neuroscience has drifted well beyond the limits of the neuron doctrine. So where will this new course lead? In 2005, 46 years after his *Science* paper shot the first hole in the doctrine, Bullock raised an intriguing question in another article in the same magazine: Why are the capabilities of the human brain so superior to those of

CHAD BAKER AND RYAN McVAY Getty Images

all other animals? The neurons in animals' brains are not all that different; even the fly exploits the same neurotransmitters. Careful anatomical study does not support the notion that bigger brains or more neurons are the answer either. Bullock (who passed away in December 2005 at age 90) suggested that the answer lay in some property that allows neurons to operate as a network. Golgi would be proud.

probability that neurons will fire at the same time.

John J. Greer and his colleagues at the University of Alberta in Edmonton reported this past February that when they bathed a fetal rat in a solution that stopped all synaptic transmission, neural circuits in its spinal cord and developing brain continued to fire rhythmically and in concert. Somehow, without any neurotransmitters in motion, neurons found a way to fire coher-

The unparalleled abilities of the human mind arise not from neurons but from the coherence of brain waves.)

Bullock had begun to explore brain waves in a variety of animals as simple as crabs and as complex as dolphins. He determined that patterns of brain waves in humans differed markedly from those in simpler animals. Brain waves arise from the collective activity of thousands of neurons working together, much like the din of a crowd at a baseball stadium. When Bullock examined the power spectrum of brain waves, he saw that waves belonging to animals that appeared earlier on the evolutionary ladder tended to have more high-frequency components, whereas mammalian brain waves were shifted toward lower frequencies.

Work by Bullock and others also showed that the electrical activity in different groups of neurons is often coupled, even though the neurons are not physically connected. It is as though people in different parts of a stadium are carrying on a single, coherent conversation. This coherence of activity in brain waves increases in animals with more powerful brains. Perhaps, Bullock suggested, the unparalleled abilities of the human mind arise not as a unique property of our neurons or brain circuitry but as an emergent property of the way its billions of neurons operate cooperatively.

But how is activity in different neurons coordinated? Part of the answer may lie in a phenomenon we are all familiar with from listening to the radio. Sometimes frequencies from one radio station bleed over to the frequencies of another. Similarly, electrical signals transmitted through nearby axons are sometimes picked up as weak signals in adjacent axons. This unruly behavior, called ephaptic transmission, may be simply an unavoidable characteristic of electricity. And the brain may tap into it to coordinate brain waves. The voltages from the intruding electrical signals heighten the

ently. Using similar methods over the past 20 years, F. Edward Dudek, now at the University of Utah, has found that electrical coupling synchronizes impulse firing during brain seizures and that ephaptic transmission couples firing of neurons in the hippocampus, a part of the brain essential for memory. Ephaptic transmission, gap junctions, neuromodulators and glia are all ways of making neurons work together in groups. This cooperation increases coherent activity in the brain, and all these processes operate outside the neuron doctrine.

So both Golgi and Ramón y Cajal were right, yet neither they nor their followers succeeded in explaining the entire universe inside our heads. Furthermore, the point of the century-long debate between the doctrinaires and reticularists is not to crown a victor but to hone our thinking and inspire new experiments to explore one of nature's greatest mysteries: how the human mind functions.

The question for the future is: How are brain waves so well coordinated in the brain? To many neuroscientists, the answer lies just over the horizon, just beyond the concept of neurons acting as single functional units. Perhaps our present instruments are inadequate to provide the essential data. Or perhaps, recalling Ramón y Cajal, the answer is already here waiting for someone to see it. **M**

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BURNED OUT

**YOUR JOB IS EXTREMELY FULFILLING. IT IS ALSO
EXTREMELY DEMANDING—AND YOU FEEL
OVERWHELMED. YOU ARE NOT ALONE** BY ULRICH KRAFT

Since getting his business degree nine years ago, Larry has been the model hard-charging executive bound for the top. After the 28-year-old joined a consulting company, he was quickly promoted to a position with loads of responsibility, a company car and an enviable income. Along with the fulfilling tasks came constant travel and 60- to 80-hour workweeks, including meetings on weekends. But he did not mind. “Occasionally it occurred to me how stressful the job was,” he says. “But I really got a kick out of it. For a long time, it was lots of fun.”

Until the day he ended up in the intensive care unit. Larry collapsed right outside the door to his apartment, with a terrible headache, a racing heart and vertigo. “At first I thought I had had a stroke,” he recalls now, a year later. But the doctor’s diagnosis was different: burnout syndrome. The consultant was sick from years of excessive toil.

Larry is not unique, and many experts believe that experiences like his are occurring more frequently in an era of lean staffing. “Perhaps now more than ever before, job stress poses a threat to the health of workers,” according to a publication of the National Institute for Occupational Safety and Health, the federal agency responsible for conducting research and making recommendations for the prevention of work-related illnesses and injury. And whereas exhaustion from overwork may happen more commonly in midlife, when energies naturally begin to ebb, it can arise earlier as well. A November 2005 Harris Interac-

concrete numbers, however, the experts agree: pressure in all trades is rising, and people are struggling to cope.

It is clear that long-term strain plays a central role in burnout. Historically, the body’s stress reaction has been a useful protective response. It helps humans—and other animals—survive an immediate threat, such as the appearance of a predator. Before we are consciously aware of it, the brain recognizes a potential danger and sets in motion, in just fractions of a second, a series of physical responses that ready us to fight or flee. Epinephrine, or adrenaline, flows to muscles, in

(It tends to hit the **best employees**, those with enthusiasm who accept responsibility readily.)

tive poll commissioned by Spherion Corporation in Fort Lauderdale, Fla., found that one third of workers ages 25 to 39 already felt burned out by their jobs.

The term “burnout syndrome” was coined in the early 1970s by Herbert J. Freudenberger, a New York psychoanalyst. Freudenberger had noticed that his own job, which was once so rewarding, had come to leave him feeling only fatigued and frustrated. Then he noticed that many of the physicians around him had, over time, turned into depressive cynics. As a result, those doctors increasingly treated their patients coldly and dismissively.

Freudenberger soon began looking at examples outside of health care—and found similar cases in many professions. Afflicted people suffered from mood fluctuations, disturbed sleep and difficulty concentrating. Accompanying the mental distress were physical ailments such as backaches or digestive disorders. Freudenberger defined burnout syndrome as a state of mental and physical exhaustion caused by one’s professional life.

No specific statistics track the ailment, partly because burnout syndrome does not have its own classification in the *Diagnostic and Statistical Manual of Mental Disorders*—the bible of the field. Rather it falls under a category of “undifferentiated somatoform disorder.” Even without

preparation for battle or running. Our senses sharpen. The body shuts down nonessential systems, such as digestion, to conserve energy.

The problem? The alarm swings into action even when the menace is not a hungry-looking bear at the entrance to the cave but rather an irritable boss who wants that PowerPoint presentation finished in 30 minutes. Each time the system gets tripped—as we crunch to meet an impossible production deadline, dash to a meeting, hurriedly pack for yet another last-minute business trip—the adrenal glands secrete stress hormones, the heartbeat speeds up, and blood pressure rises. If such tensions endure for weeks, months or years, physical consequences arise inevitably. Chronic stress contributes to hypertension, heart problems and a weakened immune system, so that we get infections more often [see “Stressed-Out Memories,” by Robert M. Sapolsky; *SCIENTIFIC AMERICAN MIND*, Vol. 14, No. 5; 2004].

Vicious Cycle

For many victims of burnout, the fuel for the fire comes from similar sources. It tends to hit the best employees, those with enthusiasm who accept responsibility readily and whose job is an important part of their identity. Larry describes it well: “At a certain point my job had so consumed me that my other needs no longer counted. My overengagement in work led to a constantly worsening state of exhaustion and apathy.”

In response to mounting task loads, the wretch piles on the hours, pulling late nights at the office, ignoring exercise, skipping meals or eating unhealthful fast foods on the run, cancel-

(The Author)

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The Burnout Cycle

Burnout syndrome does not strike overnight; it develops gradually over time. Psychologist Herbert Freudenberger and his colleague Gail North have divided the process into 12 phases. The steps do not necessarily follow one another in order. Many victims skip certain stages; others find themselves in several at the same time. And the length of each phase varies from patient to patient.



A compulsion to prove oneself

STAGE 1 The beginning is often excessive ambition: their desire to prove themselves at work turns into grim determination and compulsion. They must show their colleagues—and above all themselves—that they are doing an excellent job in every way.

Working harder

STAGE 2 To meet their high personal expectations, they take on more work and buckle down. They become obsessed with handling everything themselves, which in turn demonstrates their notions of “irreplaceability.”

Neglecting their needs

STAGE 3 Their schedules leave no time except for work, and they dismiss as unimportant other necessities such as sleeping, eating, and seeing friends and family. They tell themselves that these sacrifices are proof of heroic performance.

Displacement of conflicts

STAGE 4 They are aware that something is not right but cannot see the sources of their problems. To deal with the root causes of their distress might set off a crisis and is thus seen as threatening. Often the first physical symptoms emerge at this stage.

Revision of values

STAGE 5 Isolation, conflict avoidance and denial of basic physical needs change their perceptions. They revise their value systems, and once important things such as friends or hobbies are completely dismissed. Their only standard for evaluation of their self-worth is their jobs. They become increasingly emotionally blunted.

Denial of emerging problems

STAGE 6 They develop intolerance, perceiving colleagues as stupid, lazy, demanding or undisciplined. Social contacts feel almost unbearable. Cynicism and aggression become more apparent. They view their increasing problems as caused by time pressure and the amount of work they have—not by the ways they have changed.

Withdrawal

STAGE 7 They reduce social contact to a minimum, becoming isolated and walled off. They feel increasingly that they are without hope or direction. They work obsessively “by the book” on the job. Many seek release through alcohol or drugs.

Obvious behavioral changes

STAGE 8 Others in their immediate social circles can no longer overlook their behavioral changes. The once lively and engaged victims of overwork have become fearful, shy and apathetic. Inwardly, they feel increasingly worthless.

Depersonalization

STAGE 9 They lose contact with themselves. They see neither themselves nor others as valuable and no longer perceive their own needs. Their perspective of time narrows to the present. Life becomes a series of mechanical functions.

Inner emptiness

STAGE 10 Their inner emptiness expands relentlessly. To overcome this feeling, they desperately seek activity. Overreactions such as exaggerated sexuality, overeating, and drug or alcohol use emerge. Leisure time is dead time.

Depression

STAGE 11 In this phase, burnout syndrome corresponds to depression. The overwhelmed people become indifferent, hopeless, exhausted and believe the future holds nothing for them. Any of the symptoms of depression may be manifest, from agitation to apathy. Life loses meaning.

Burnout syndrome

STAGE 12 Almost all burnout victims now have suicidal thoughts to escape their situation. A few actually carry them out. Ultimately, they suffer total mental and physical collapse. Patients in this phase need immediate medical attention.

ing personal dates with friends, missing the kids' soccer games. Ultimately, Larry relates, "I completely isolated myself." Humans are social beings, so we do not fare well when cut off from such networks. "Support from family, friends and colleagues is a vital buffer against stress," says Manfred Schedlowski of the Swiss Federal Institute of Technology in Zurich, which has recently created a research group to study the

utterly depleted overnight; on the contrary, their batteries run down so gradually that many of them never notice the subtle changes until things are dire. Working long hours, through weekends, they think, "No problem—I am just a little tired right now." But then there is the first time they cancel the tennis game or mumble "sorry" about missing that long-planned weekend trip with friends. The mountain of papers waits on the desk.

If someone works 12 hours a day, every day, yet still has found a way to relax, he will very likely have no problem.

causes and consequences of work-related stress.

Another risk factor is the level of control a person has over his or her work and the recognition (or lack thereof) that endeavors receive. Juergen Staedt, a psychiatrist who runs the Vivantes Clinic in Berlin, speaks of a woman who was a successful department head for years—until a corporate restructuring during which she was, despite her desperate efforts, unable to prevent layoffs among her employees. It was a slap in the face for her. Plagued by sleep disturbances, loss of appetite and feelings of low self-worth, she ended up at Staedt's clinic. "Such setbacks are a part of life. But people with burnout-syndrome personalities simply can't work their way past them," he explains. "Their entire self-image is shattered." The experts call such stumbles gratification crises—the feeling that their tremendous hard work on the job is not sufficiently noticed—and they add to the problem.

Sooner or later, the ability of these victims to work declines. They find it hard to concentrate, they have few creative ideas, and their memories often fail. They begin to make mistakes. "Then the vicious spiral begins," Staedt explains. "Noticing that you are no longer doing good work increases the pressure on you, and things go from bad to worse." The once generous Larry, for instance, blamed colleagues for his own mistakes and began to criticize and scold them.

Stress and self-dissatisfaction leave their marks on the psyche. Resigned, discouraged, plagued by flagging self-esteem and anxiety about failure, people with burnout syndrome drag themselves painfully through each day. They may seek solace in alcohol or pills. Some even attempt suicide.

The victims are often the last to realize the seriousness of their situation. No one becomes

They cannot leave the work undone, can they?

"Of course, I was aware that things were not going well. But I thought I would deal with it somehow," Larry recalls. When he finally collapsed on his doorstep, he realized at last that he needed help: "That was the shot across the bow that rescued me."

Staedt provides a metaphor for this problem: "If you own a car, you have it inspected each year and you check the oil regularly. Burnout-syndrome patients never bring their 'cars' in for inspection. They drive thousands of miles at full speed and then are shocked when the motor suddenly fails. They have been neglecting routine maintenance."

This inability to find meaning in life outside of work is why advice to just ease up a bit and turn your computer off by five does not work for burnout-syndrome patients. Anyone who hopes to overcome the problem has to learn that satisfaction can come from things other than job success. That is where psychiatrist Staedt comes in. "What we do is something like enjoyment training," he says. "The patients learn how, at last, to do something merely for the pleasure it provides. Baking cookies, painting and taking walks are just as much a part of the therapy as sports and talking to other people."

This is the crux of the matter, Schedlowski believes. "The personality characteristics that have, till now, guaranteed your professional success are what you must now say good-bye to." In treating his exhausted execs, the psychologist can often trace these "master plans" back to the patients' childhoods. "People who, for example, learn as kids always to be punctual, and always do everything perfectly, will profit from that later," he points out. With such ingrained virtues, they did well in school, and later in their careers

they rose quickly. Now they also need to master new skills—healthier ones.

This “rewriting the master plan” is the most difficult part of the therapy. It has to do with how the brain functions. Things learned early, and practiced dutifully, become firmly anchored in our brains. “Relearning habits and ways of behavior that are so strongly ingrained is a training process that takes time,” Schedlowski states. He recommends six months of ambulatory therapy, during which the patients practice their new, better routines repeatedly in daily life.

Putting on the Brakes

It would be far better never to fall into the vicious cycle of overwork and inner pressure in the first place. The Zurich team is working to counter this eventuality through educational programs. “Stress has become almost normal in today’s business world,” Schedlowski observes. “If you know how to protect yourself against its effects, the risks of burning out are much lower.”

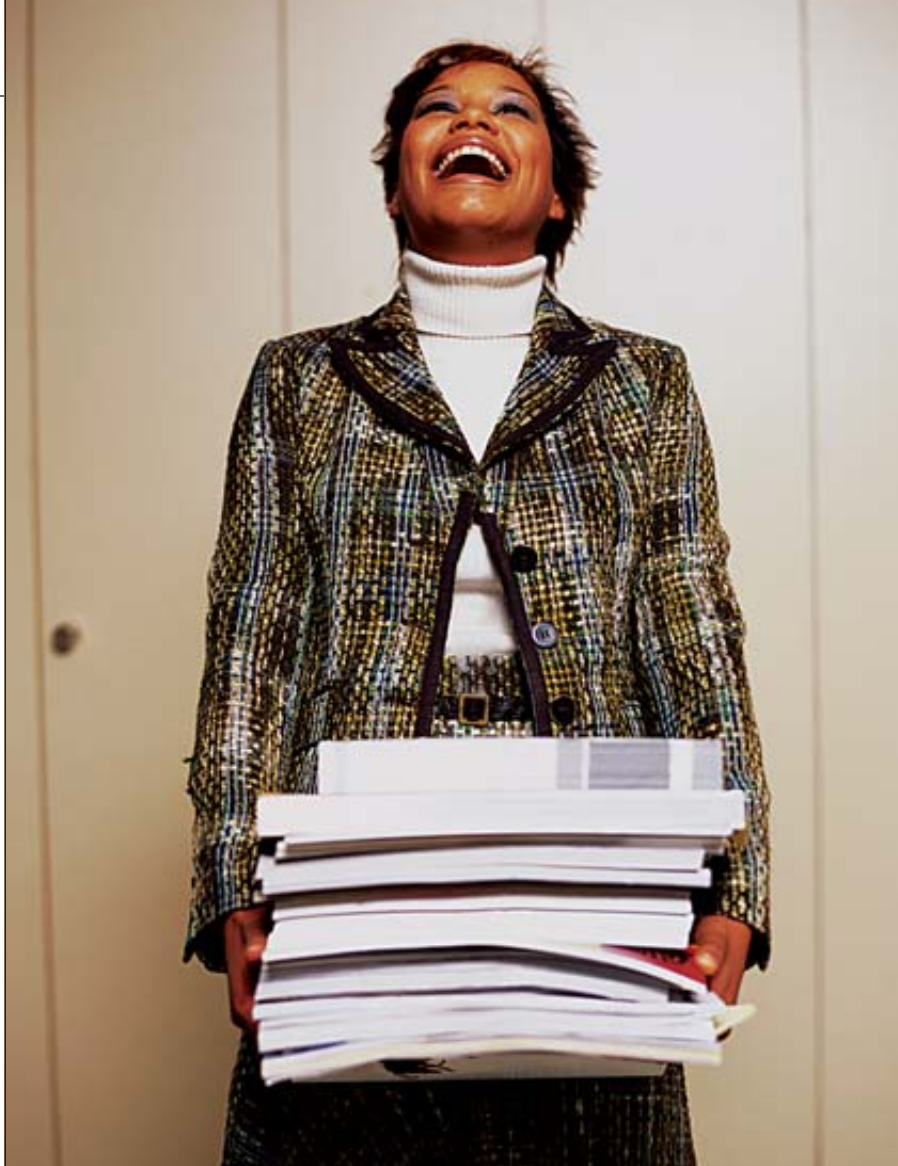
The quantity of stress is a determinant but not the decisive one. “If someone works 12 hours a day, every day, yet still has found a way to relax, he will very likely have no problem,” Staedt explains. “On the other hand, someone else may find a part-time job extremely stressful—and develop burnout syndrome.”

Rule number one: budget your physical resources. The antistress measures that are involved are as simple as they are effective. They include eating wholesome foods at mealtimes, exercising regularly and getting enough sleep.

Rule number two: workaholics must aim for equilibrium between tension and relaxation. Or, in the language of those in the field, find their work-life balance. “Everyone has to find their own stress-compensation mechanism,” Schedlowski says. One woman may reduce stress by running long distances, whereas another may lie on her sofa at home listening to classical CDs, and still a third may tend the rose bushes in her garden. The hobby itself doesn’t matter; it is devotion to a pleasurable activity that does.

Close social contacts are also important [see “Good Friends,” by Klaus Manhart; *SCIENTIFIC AMERICAN MIND*, April/May 2006]. Spending time with friends, family, even colleagues at work, protects against excessive stress. Last, it is helpful to learn some relaxation technique, such as yoga or progressive muscle relaxation.

The decisive step, Schedlowski emphasizes, must be made first in your head. “As early as possible in your professional career, you must absorb



the idea that physical and mental health are at least as important as climbing the ladder toward success,” he says.

Ultimately, Larry made the switch to a more balanced existence. He resigned from his job, repaired his friendships and fulfilled a boyhood dream by taking a round-the-world trip. Then he returned to being a consultant, landing a better spot than the one he had left. But now he balances labor with “more sports, more leisure time, more downtime, more time to enjoy life. Even though my job is, as before, important to me, these things have priority now.” He likes the result. “Things have never been better!” **M**

Workloads seem lighter when countered by antistress measures such as exercising, enjoying time with friends and cultivating a hobby.

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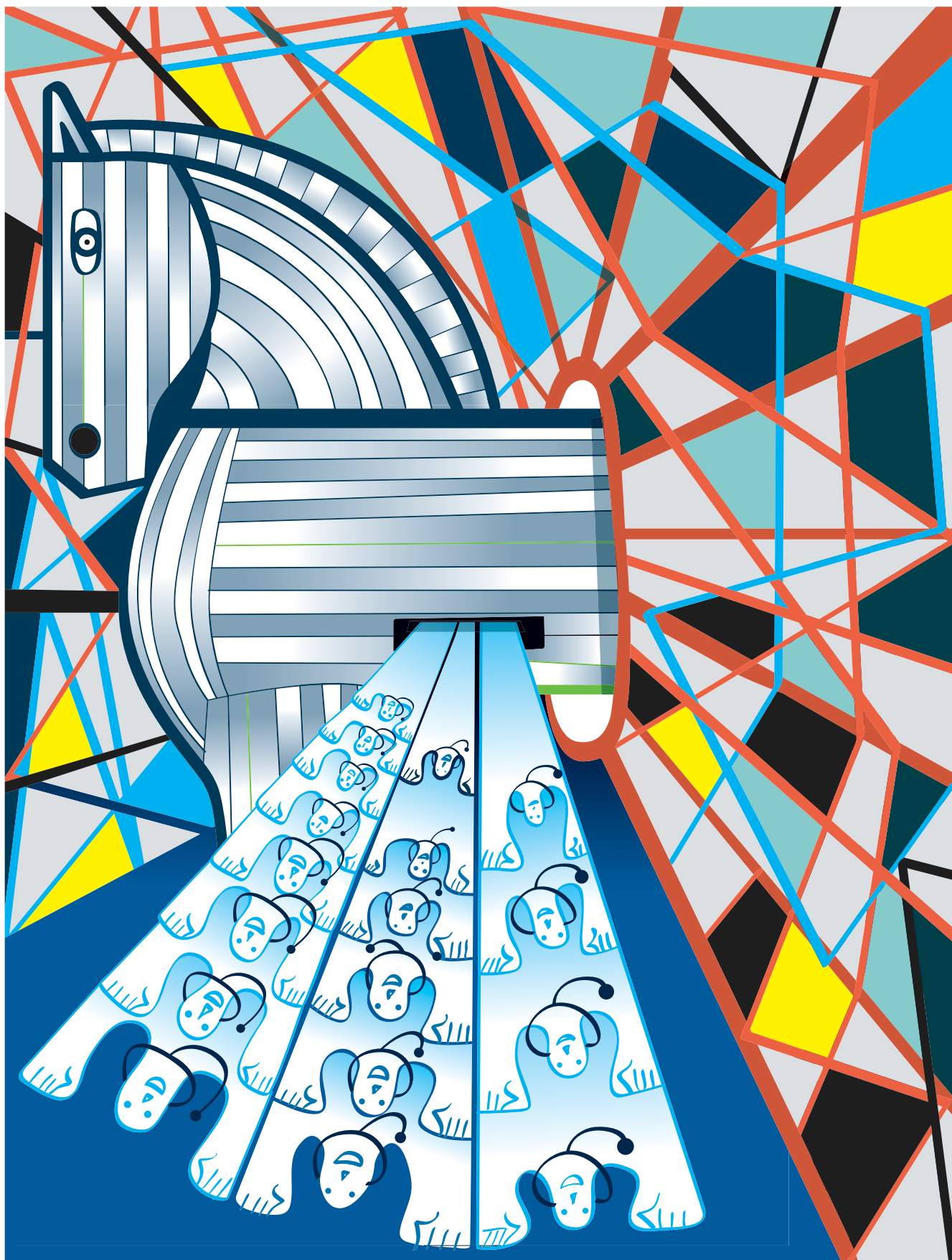
To treat neurological illnesses, researchers are learning how to smuggle drugs past the shield that guards the brain against infection

Crossing the **BARRIER**

By Grit Vollmer

Paul Ehrlich had just injected aniline dye—used to color blue jeans—into a rat’s bloodstream. For years the immunologist had been working on ways to stain cells so they would be more visible under a microscope, and aniline looked promising. Soon all the animal’s muscles, blood vessels and organs were deep indigo. But for some confounding reason the central nervous system—the brain and spinal cord—remained untouched.

Ehrlich’s experiment, done at Berlin’s Charité hospital in 1885, provided early evidence for the blood-brain barrier—a vital wall that controls which molecules in the bloodstream can enter the brain or nerve pathways. Oxygen, sugars and amino acids are allowed in; most compounds are kept out. As a result, the brain can do its job inside a secure perimeter not available to any other organ. Which is handy, because substances in air, water and food—as well as toxins and even the body’s own hormones—can severely impair the brain’s functioning. Easy



Penetrating the Wall

A sophisticated blood-brain barrier regulates which substances in the bloodstream gain access to the brain and which do not. Tiny capillaries (*far right*) are sheathed in a layer of endothelial cells, which stand shoulder to shoulder to form the wall (*below*). Dense aggregates of protein, called tight junctions, weld adjacent cells so no molecule can pass between them. To reach the brain, a substance must travel through an endothelial cell body itself.

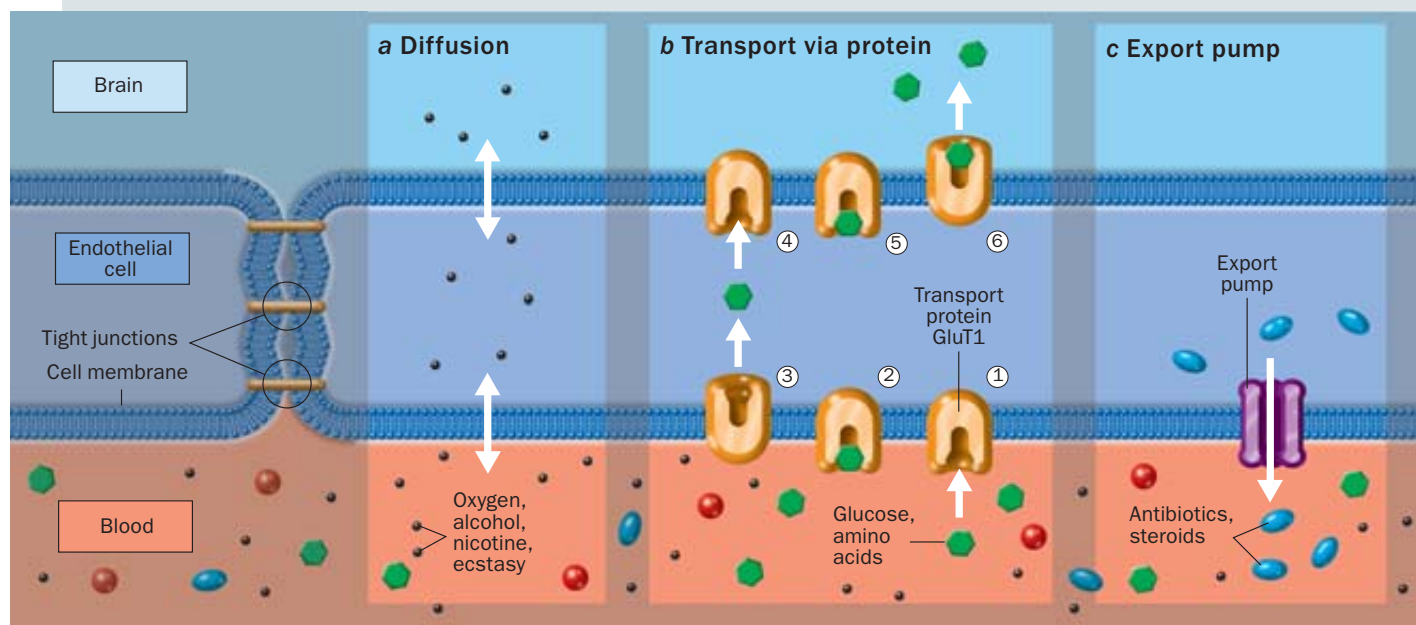
Gases such as oxygen and carbon dioxide are so small they can diffuse across these cells unhindered (*a*). And because the endothelial cell membrane contains lipids, small molecules that have a strong affinity for lipids can slip through, which is how alcohol, nicotine, caffeine, ecstasy and heroin are able to get in to disturb brain function.

Lipids repel molecules that dissolve in water, however. These and larger molecules in general—including glucose, amino acids and vitamins—require special

transport systems (*b*). The GluT1 protein, for example, carries glucose into the brain. The sugar molecule first binds to the transport protein in the endothelial membrane (1), which then changes shape (2) to release the glucose within the cell (3). The sugar docks to a GluT1 protein on the other side (4), which transports it into the brain (5, 6).

Compounds that dissolve in lipids—among them useful drugs such as antibiotics, steroids, and beta blockers—would seem to enjoy easy passage. But export pumps sense these substances as foreign and expel them from the endothelial cell back into the bloodstream (*c*). To date, 15 such pumps have been discovered, many of which keep toxins out of the brain.

Another mechanism vital to transporting especially large compounds, such as iron and insulin, is receptor-mediated transcytosis (*d*). In one case, the protein transferrin latches onto iron in the blood. The transferrin then binds to a receptor in the endothelial cell membrane (1).



access would quickly lead to mental chaos.

This brilliant defense can be a cursed impediment to curing brain diseases, however. Almost no therapeutic drugs can penetrate the blockade. William Pardridge, professor of medicine at the University of California, Los Angeles, says 98 percent of drugs that have some effect on the central nervous system cannot cross into the brain. Pharmaceuticals cannot battle meningitis, rabies, tumors, Alzheimer's or multiple sclerosis, because they cannot reach the sites where the dis-

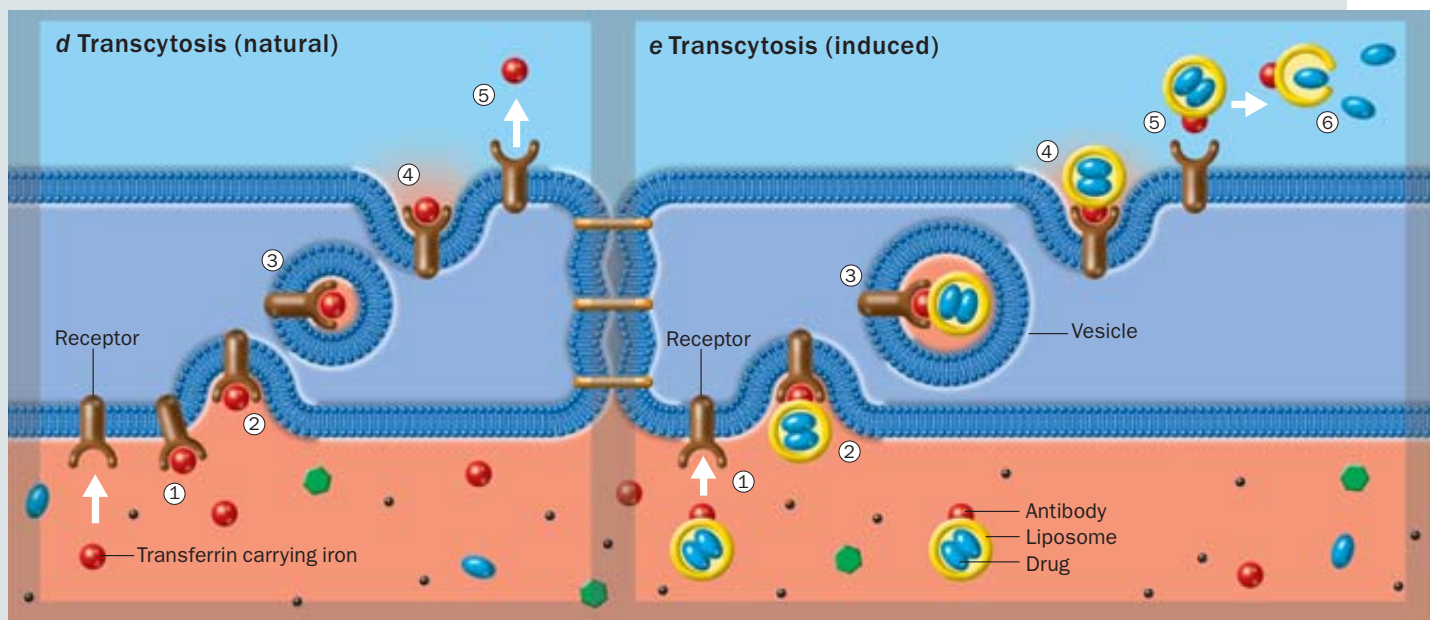
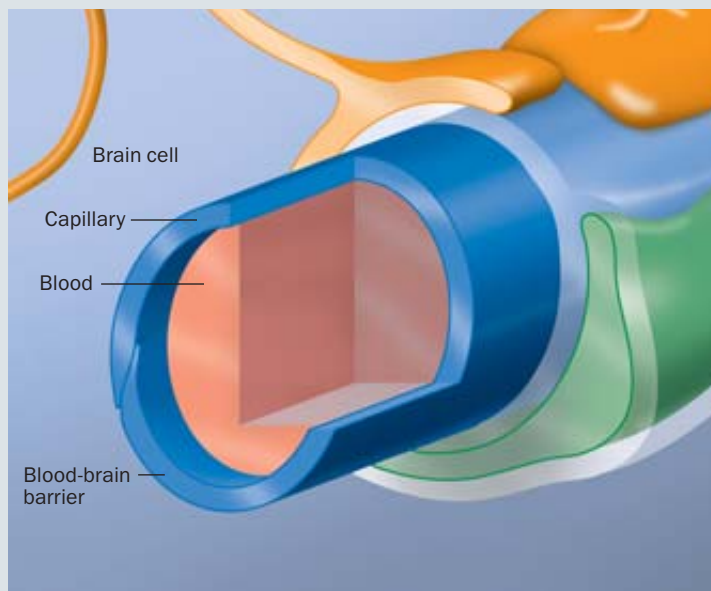
eases are wreaking havoc. Nevertheless, scientists have greatly improved their understanding of the sophisticated mechanisms the blood-brain barrier uses to grant or deny admission, and they are devising ways to exploit those mechanisms to sneak therapeutic drugs through.

No Trespassing

It can be hard to visualize the blood-brain barrier. It is not a filter at the base of the head or an envelope surrounding the brain and spinal

As the receptor backs in (2), a part of the membrane transforms itself into a vesicle containing the transferrin and iron (3). This vesicle fuses with the membrane on the opposite side (4), so that transferrin can release the iron into the brain (5).

Researchers are trying to exploit transcytosis to deliver therapeutic drugs that the barrier would otherwise block or expel (e). Special drug taxis, like Trojan horses, can smuggle their cargo through the wall. A scientist fills a tiny liposome (a fatty complex) with drug molecules and attaches an antibody that will fit into a transferrin receptor, fooling the receptor into treating the cargo as a natural one. The receptor accepts the antibody and liposome (1), which are enveloped in a vesicle (2, 3) that passes them into the brain (4, 5). There the liposome releases the drugs (6). —G.V.



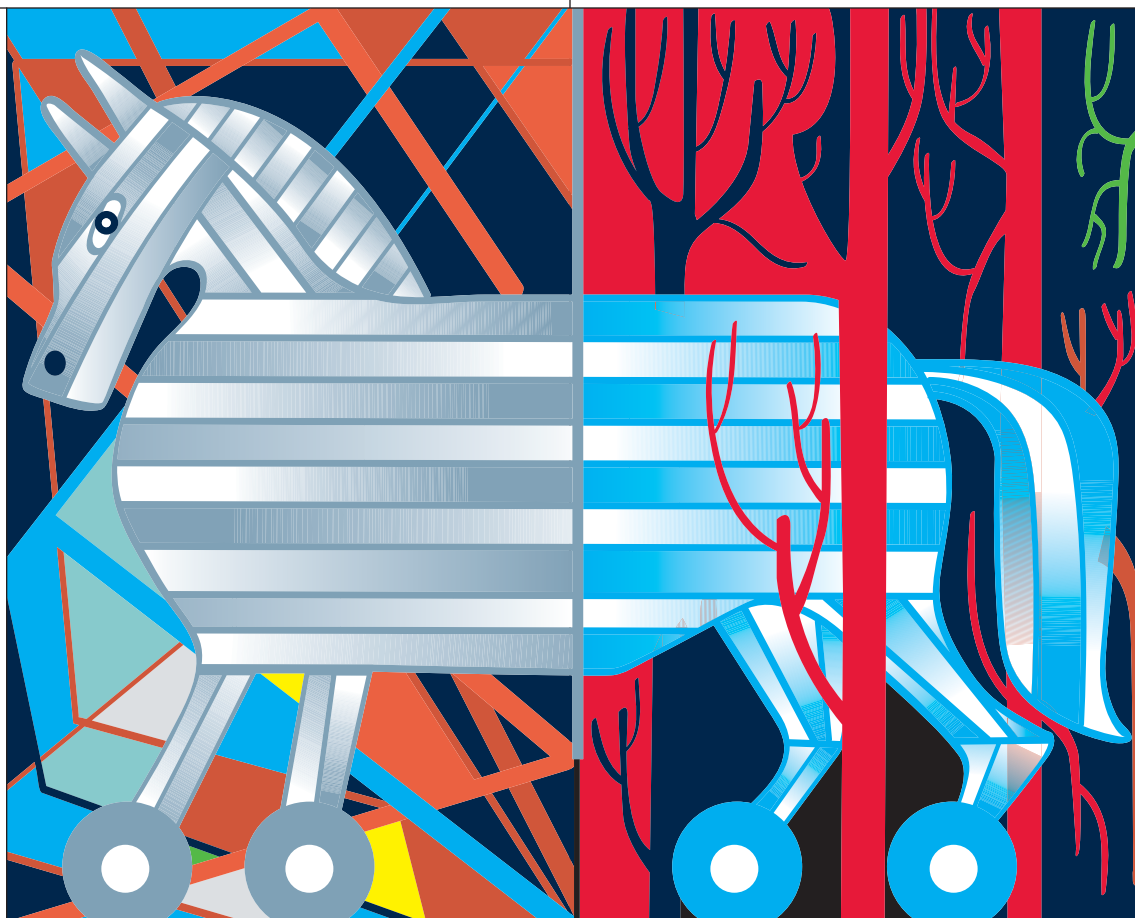
cord. It is a layer of special, tightly knit cells—a carpet—that lines the inner walls of all the small blood vessels that reach into the brain and spinal cord. Like soldiers standing shoulder to shoulder, these endothelial cells allow only certain molecules to pass from the blood on one side of them into the region of nerve cells on the other.

Thomas Reese and Morris Karnovsky, faculty members at Harvard Medical School, first made the blood-brain barrier visible in 1967, using an electron microscope. They discovered en-

dothelial cells tightly packed along the blood vessel walls. Tough proteins tie each endothelial cell to its neighbors, filling the space between them so nothing can squeeze through. (In blood vessels serving other organs, the endothelial cells are loosely connected, so substances can readily

(The Author)

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slide between them.) The only way that a molecule in the bloodstream can reach the nerve tissue is to pass right through the endothelial cell bodies themselves.

Of course, the brain cannot be completely shut out. Its cells need nutrients to survive and function correctly. Because of their tiny size, molecules such as oxygen can diffuse right through the guard cell bodies. But so can alcohol, nicotine, heroin and the party drug ecstasy [see box on preceding two pages]. Larger molecules such as glucose are funneled in through selective gates, and others such as iron are cloaked inside special transporters that ooze through the cells.

A few substances, especially ecstasy, actually damage the barrier as they cross it. Bryan Yamamoto, a pharmacology professor at Boston University, gave the party drug to rats, then injected them with a dye that is normally too large to cross the blood-brain barrier. The dye easily reached the brain. The rats received no more ecstasy, yet even 10 weeks later newly injected dye still was able to enter the brain. The ecstasy had made the blood-brain barrier far more permeable for an extended time—exposing the brain to pathogens. Yamamoto cannot say how long the drug's effect lasts in humans, but 10 weeks in a

rat's life corresponds to five to seven human years.

Certain viruses and bacteria, such as those causing rabies, meningitis and cholera, trick the blood-brain barrier by attacking proteins on the endothelial cells, forcing open the gates. Brain tissue may then become dangerously inflamed, but there is at least one positive consequence: the swelling weakens the barrier, making it a bit easier for immune system cells to push through and fight the infection.

In the case of multiple sclerosis, the same mechanism goes out of control. Hordes of immune cells shove their way into the brain, exacerbating the inflammation reaction. Multiple sclerosis is indeed a disease of the blood-brain barrier; only after immune cells are suddenly able to flood across the border do they attack the myelin sheaths around nerves. These sheaths insulate the nerves, enabling them to conduct signals quickly and cleanly; as myelin is destroyed, nerve impulses become erratic and destructive.

Trojan Horses

Many therapeutic drugs that might fight brain diseases are simply too large to diffuse through unnoticed, the way ecstasy and heroin do. Ironically, another defense mechanism thwarts

(Alkylglycerols open the barrier for just a few minutes so medication can cross. Then the wall closes.)

the transport of even small medications past the barrier. So-called export pumps snare “foreign” molecules as they begin to cross the endothelial cells and expel the invaders back into the bloodstream. Scientists are therefore devising tricks to sneak drugs around the export pumps or temporarily disable them.

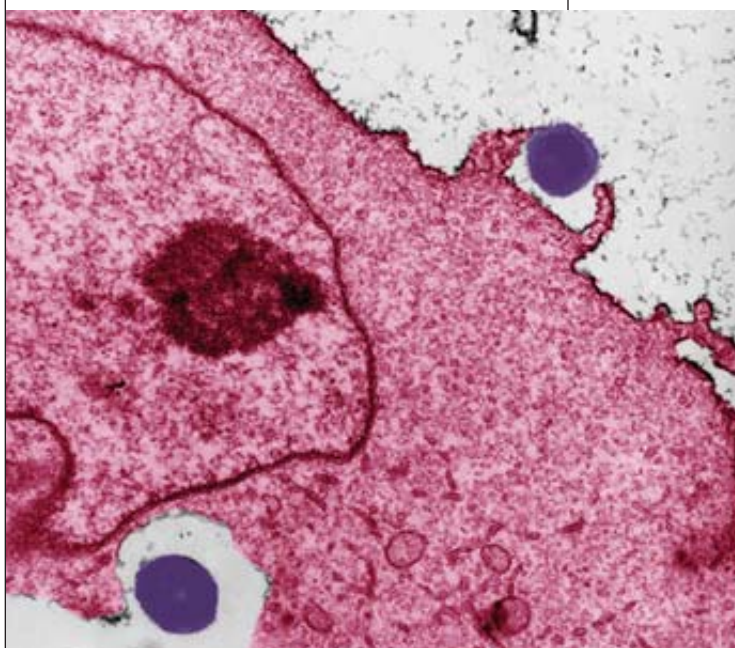
Researchers at the University of Veterinary Medicine in Hannover, Germany, have constructed a blocking molecule that binds to a protein that operates the pumps, preventing the protein from initiating the pumping action. In rats the inhibitors make the barrier more permeable. Initial tests on epilepsy patients have reduced the number of seizures related to overactivity of the pumps.

A basic problem exists with this general approach, however. Disabling the export pumps in the brain also disables the pumps in linings that protect other organs throughout the body, exposing them to influxes of harmful substances that are normally rejected. Therefore, Gert Fricker, a biochemist at the Institute for Pharmacy and Molecular Biotechnology at the University of Heidelberg in Germany, is trying a different scheme: devising disguises for drugs.

Fricker and his team are crafting tiny, hollow spheres called liposomes that will sneak drugs through the wall like Trojan horses. The spheres are made of lipids—fatty complexes—and slide through the lipid-embracing epithelial cells while holding drug molecules inside their hollow cores. He is also tacking natural antibodies onto the outsides of liposomes that can latch onto receptors in the wall that will, in turn, pull the liposome through [see box on pages 36 and 37]. At U.C.L.A., Pardridge has had similar successes. Victor Shashoua, formerly a biomedical researcher at Harvard Medical School, has used a fatty acid to sneak in dopamine, a neurotransmitter that is lacking in several brain illnesses, such as Parkinson’s disease.

Doctors already use such Trojan horses—sometimes called drug taxis—to deliver medication to other organs, for example, to fight stomach cancer. For brains, researchers have used this method only on lab animals thus far; clinical human studies are still in the planning stage.

Fricker’s team is also working on alkylglycerols with the National Institute of Environmental



Health Sciences in Research Triangle Park, N.C. These molecules are soluble in both lipids and water and in limited tests have succeeded in opening the barrier to chemotherapeutic compounds. For reasons that are not fully understood, the alkylglycerols open the vital barrier for just a few minutes so the therapeutic agents can cross. Then the wall seems to close naturally again. The short span of permeability would make it less likely that dangerous molecules could also reach the brain, the way ecstasy is allowed in. Experimenters at U.C.L.A. and at Ohio State University have introduced anticancer compounds into a rat’s bloodstream that open up only the part of the barrier that is close to a brain tumor.

These advances and others are giving scientists hope that one day doctors will have a full bag of tricks they can use to exploit the blood-brain barrier. In these cases, the brain won’t mind being fooled. **M**

Bacteria (purple) that cause meningitis transport through the blood-brain barrier, as observed by researchers at the University of California, San Diego.

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SEEING IN



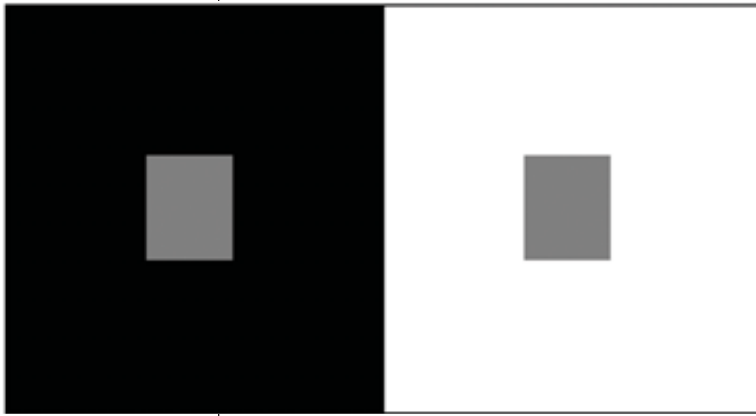
BLACK & WHITE

Why
it's not so
cut-and-
dried

By Alan Gilchrist

How many times have you heard people say that something is “black and white,” meaning it is simple or crystal-clear? And because black and white are so obviously distinct, it would be only natural for us to assume that understanding how we see them must be equally straightforward.

We would be wrong. The seeming ease of perceiving the two color extremes hides a formidable challenge confronting the brain every time we look at a surface. For instance, under the same illumination, white reflects much more light to the eye than black does. But a white surface in shadow



The gray rectangle in the black panel appears lighter than the identical gray surrounded by white.

To learn what the brain uses as an “anchor” against which to judge various patches of gray in images, the author and his colleagues built a dome with its interior painted half black and half gray. Volunteers who peered inside saw the gray side as white and the black side as gray—proving that the brain’s anchor is the lightest shade in a scene.



often reflects less light to the eye than a black surface in sun. Nevertheless, somehow we can accurately discern which is which. How? Clearly, the brain uses the surrounding context to make such judgments. The specific program used to interpret that context is fraught with mystery for neuroscientists like me.

Recent studies of how we see black and white have provided insights into how the human visual system analyzes the incoming pattern of light and computes object shades correctly. In addition to explaining more about how our own brains work, such research could help us in the design of artificial visual systems for robots. Computers are notoriously horrible at the kind of pattern recognition that comes so naturally to people. If computers could “see” better, they could provide



more services: they could recognize our faces for keyless locks, chauffeur us around town, bring us the newspaper or pick up the trash.

Ask the Brains

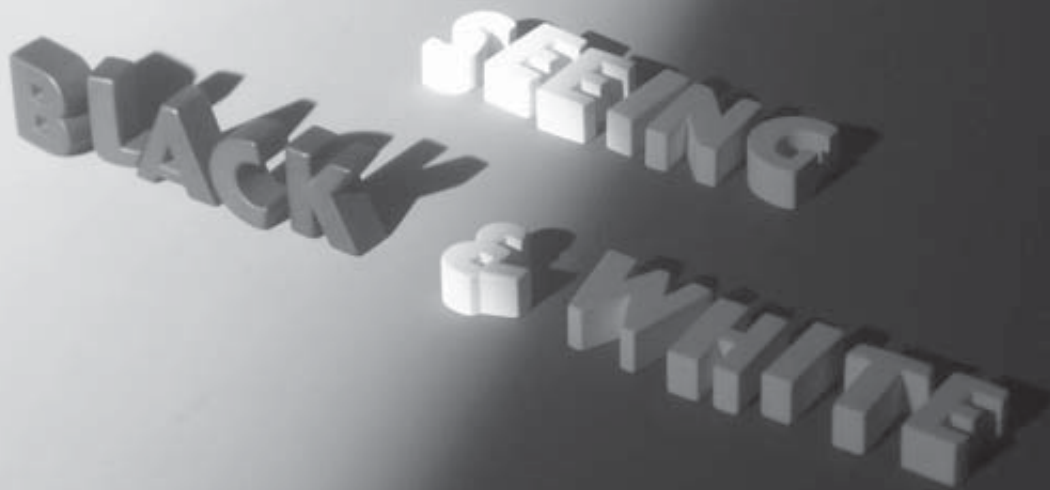
Vision scientists force the brain to reveal its secrets using a method called psychophysics. Of course, the brain is not going to talk to us in lucid prose. Rather it is like a game of 20 questions. We ask the brain only yes or no questions: Do you work this way or that way? To get a clear answer, we must start with at least two competing hypotheses. Then we must carefully construct a test image that contains a critical “target” surface that should appear, let us say, light gray according to one hypothesis but dark gray for a competing explanation. Often these test images consist of delightful illusions, such as those you will see in this article.

To appreciate the complexities of seeing a surface as black, white or gray, it helps to start with some basic physics. White surfaces reflect most of the light that strikes them—roughly 90 percent. In contrast (pun unintended), black surfaces reflect only about 3 percent of that light. When this reflected light enters the eye opening called the pupil, the lens focuses it onto the inner rear surface, or retina, much as light enters a simple box camera through a lens and then strikes the film. Photoreceptors in the retina can measure the amount of incoming light striking them.

So far, so good. But the light reflected from an object we look at, by itself, contains no hint of the shade of gray from which it was reflected. Here is where things get interesting.

The total amount of light reaching the eye depends far more on the level of illumination in any scene than it does on the percentage of light that any given surface reflects. Although a white surface reflects about 30 times as much light as a neighboring black shape in the same illumination, in bright sunlight that same white surface can reflect millions of times more light than it does in moonlight. Indeed, a black surface in bright light can easily send more light to the eye than a white surface in shadow. (This fact is why no robot today can identify the gray shade of an object in its field of view. The robot can measure only the amount of light that a given object reflects, called luminance. But, as is now clear, any luminance can come from any surface.)

Recognizing that the light reflected by the object itself contains insufficient information, psychologist Hans Wallach suggested in 1948 that the brain determines a surface’s shade of gray by com-



Context matters: The “white” letters are actually darker than the “black” letters (*above*), as is clear when surroundings are removed (*inset*).

paring the light received from neighboring surfaces. Wallach, a cousin of Albert Einstein, contributed a great deal to our knowledge of visual and auditory perception in studies he conducted during his long tenure at Swarthmore College. He showed that a homogeneous disk could appear as any shade between black and white simply by changing the brightness of the light surrounding it, even though the disk itself never changes.

In a classic illusion, a gray square sits on a white background and an identical gray square is on an adjacent black background [*see top illustration on opposite page*]. If the perceived lightness depended solely on the amount of light reflected, the two squares would look identical. The square on the black background looks lighter—which shows us that the brain compares neighboring surfaces.

More recent evidence has shown that this comparison of neighboring surfaces may be even simpler than Wallach imagined. Instead of measuring

the intensity of light at each point in the scene, the eye seems to start by measuring only the change in luminance at each border in the scene.

Wallach’s work showed that the relative luminance of two surfaces is an important piece of the puzzle. But knowing just that property would still leave a lot of ambiguity. Put another way, if one patch of a scene is five times brighter than a neighboring patch, what does that tell the eye? The two patches might be a medium gray and black. Or they could just as well be white and gray. Thus, by itself, relative luminance can tell you only how different two shades are from each other but not the specific tint of either. To compute the exact gray of a surface, the brain requires something more: a point of comparison against which it can measure various hues, which researchers now call an anchoring rule.

Two anchoring rules have been proposed. Wallach himself, and later Edwin Land, inventor of instant photography, suggested that the highest

(The specific program used to interpret context
is **fraught with mystery** for neuroscientists.)



Three identical disks
pasted onto the
photograph appear
as different shades in
different locations—
showing how the
brain applies a
different anchor
within each region
of illumination.

luminance in the scene automatically appears white. If true, this rule would serve as the standard by which the brain compared all lower luminances. Adaptation-level theory, created in the 1940s by psychologist Harry Helson, implied that the average luminance in a scene always appears middle gray. Lighter and darker gray shades would then be identified by comparing other luminances to this middle value. Those working in machine vision called this the “gray world assumption.”

Which was right? In my laboratory we sought to find out in 1994. My colleagues and I at Rutgers University devised a way to test these rules under the simplest possible conditions: two gray surfaces that fill the entire visual field of an ob-

server. We asked volunteers to place their head inside a large opaque hemisphere with its interior painted a medium shade of gray on the left and black on the right. We suspended the hemisphere within a larger rectangular chamber with lamps that created diffuse lighting for the viewer.

Remember, the brain does not yet know what these two shades of gray are—it has only relative luminance. If the brain’s anchoring rule is based on the highest luminance, then the middle gray half should appear white and the black half should appear middle gray. But if the rule is based on the average luminance, then the middle gray half should appear light gray, whereas the black half should appear dark gray. The viewer

ALAN GILCHRIST

would not see either side as being black or white.

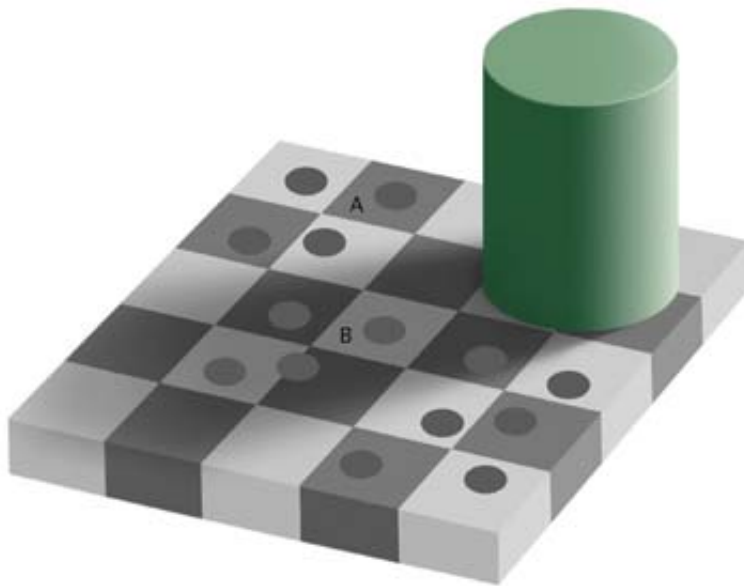
The results were clear. The middle gray half appeared totally white; the black half, middle gray. Thus, our perceived gray scale is anchored at the “top,” not in the middle. This finding tells us much about how the brain computes gray shades in simple scenes. The highest luminance appears white, whereas the perceived shade of gray of a darker surface depends on the difference—or, more precisely, the ratio—between its own luminance and that of the surface with the highest luminance.

Different Anchors

What about the much more complex scenes typical of everyday life? Does this simple algorithm work? At this point, the reader may not be surprised to learn that the answer is, “No, it is more complicated.” If the brain compared only the luminance of each surface with the highest luminance in the entire scene, then a black surface in bright light would appear as the same shade as a white surface in shadow, given only that both have the same luminance, as often happens. But they do not: we can discern the difference between them. The visual system must, then, apply a different anchor within each region of illumination.

And indeed, research with many illusions shows that the anchor does vary. If I paste several identical gray disks onto a photograph with lots of brighter areas and shadows, the disks in the shadowed regions will appear much lighter than those in the sunlight [*see illustration on opposite page*]. I call these “probe disks,” because they allow us to probe how the visual system computes gray shades at any location in the scene. Within any given region of illumination, the precise location of the disk matters little; the disk appears roughly the same shade of gray throughout the region.

Functionally, each region seems to have its own anchor—the luminance at which the brain perceives that a surface appears white. But programming a robot to process the image in this way presents a big challenge. Segmenting the picture into separate regions that have different illuminations requires the visual system to determine which edges in the image represent a change in the pigment of the surface and which, like the line formed by the outline of a shadow, mean an alteration in the illumination level. Such a program, for example, might classify an edge as the boundary between different regions of illumination if it is blurred or if it represents a planar break as, say, a corner.



Theorists such as Barbara Blakeslee and Mark McCourt of North Dakota State University argue that the human visual system need not use this kind of edge classification either. They argue for a less sophisticated process called spatial filtering. In our picture with gray disks, for instance, they would suggest that the gray shade of each disk depends mainly on the local luminance contrast at the edge of that disk (much as in Wallach’s earlier proposal). They might note that the apparent shade of each disk in the photograph depends simply on the direction and strength of the luminance contrast between each disk and its immediate background.

We can test whether this simple idea works by placing some probe disks on a checkerboard with a shadow falling across it [*see illustration above*]. We find that disks with identical local contrasts will appear to have different shades. On the other hand, disks with different local contrasts may share the same shade of gray.

All Together Now

Consider another visual trick, which sheds light on how the brain decides what elements to group together when it is sorting out patterns of light. Imagine a black “plus” sign, with two gray triangles [*see top right in box on next page*]. One of the triangles fits into the crook of the white

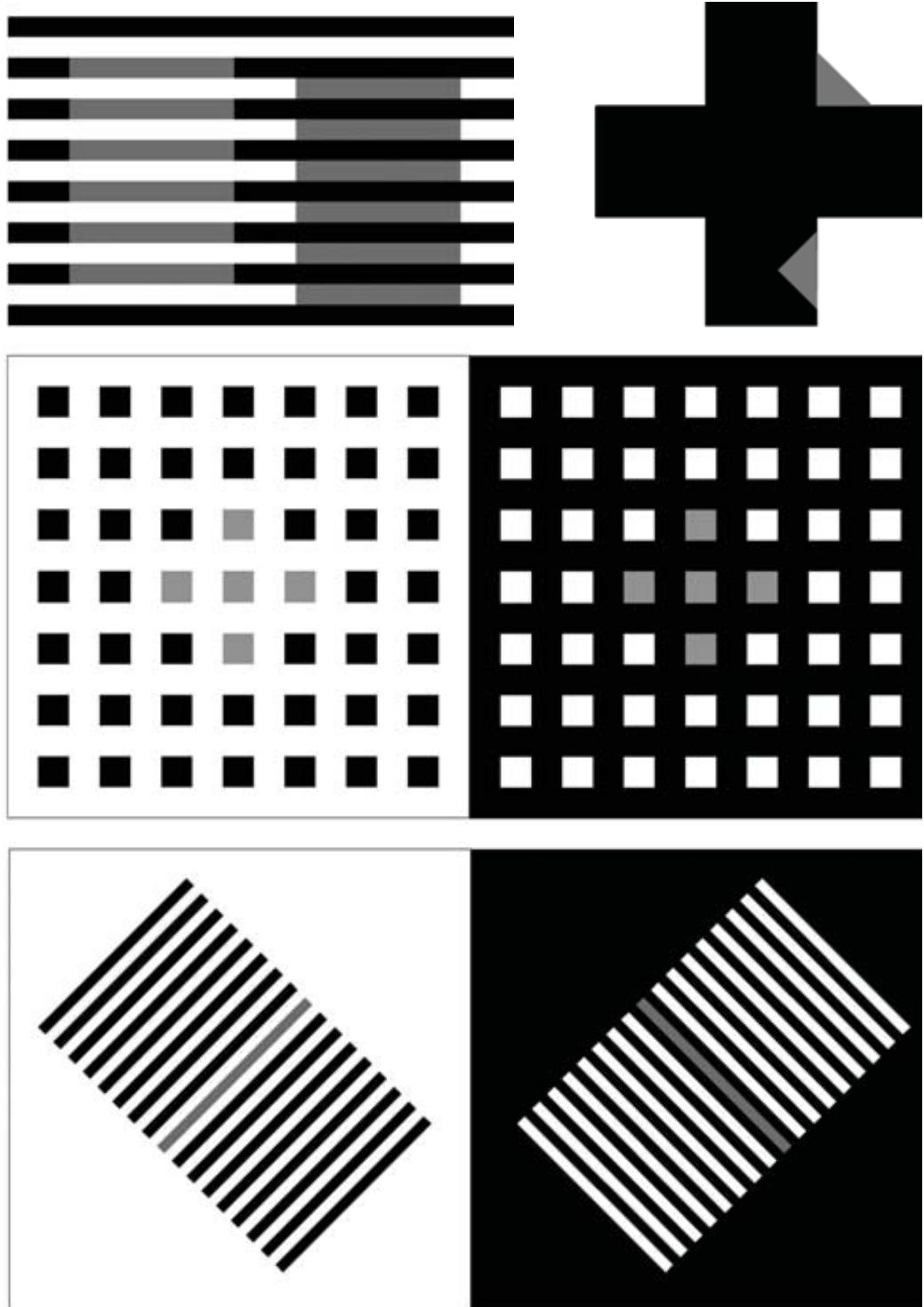
All the disks are identical, yet those in the shadow appear lighter gray. Disks on squares A and B appear to be different shades of gray, although they have identical local contrasts (squares A and B are identical in luminance, although they do not appear to be). Yet the two disks to the left and right of the letter B look the same (but have different local contrasts).

(The Author)

ALAN GILCHRIST is a professor in the psychology department at Rutgers University. He studies visual perception, especially the “software” the visual system uses to decode the retinal image. He is also interested in child raising and critical thinking. His new book, *Seeing Black and White*, a 20-year effort, is due out this spring.

The Power of Groups

In each of the illusions below, identical gray regions appear different, depending on juxtapositions with their black or white surroundings. These effects cannot be attributed solely to contrast between neighboring regions, because contrast alone typically would make us perceive gray surrounded by white as darker than gray surrounded by black. Instead the critical factor for the brain's judgment of the gray shade seems to be which regions "belong" to one another.



MICHAEL WHITE (top left); MAX WERTHEIMER AND WILHELM BENARY (top right); PAOLA BRESSAN Padova University (middle); ELIAS ECONOMOU University of Crete (bottom)

(Step by step, we will force the visual system to give up its secrets.)

area formed by the “elbow” of the plus; the other pokes inside the black area of one of the black bars. Here the two gray triangles are identical and their immediate surroundings are identical. Each triangle borders white along its hypotenuse (the longest side) and black along the other two, equal-length sides. But the lower triangle, inside the black bar, “belongs” to the black cross, whereas the upper triangle seems to be part of its white background. Notice the boundary intersections. When the borders come together to form a kind of T junction, the brain seems to define the regions divided by the stem of the T as belonging together, but not the regions divided by the top of the T.

This interpretation of T junctions as a way for the brain to establish groups holds for another illusion, created by Australian artist Michael White. It has a series of horizontal black bars stacked with white spaces between them. In it, gray bars that are neighbored by black more than by white [see top left in box on opposite page] appear darker (not lighter) than the gray bars that are neighbored mostly by white. Here the T junctions at the corners of the gray bars suggest that the gray bars on the left lie in the same plane as the white background, whereas those on the right lie in the same plane as the black bars.

Paola Bressan in the psychology department at Padova University in Italy created a “dungeon” illusion, which further details the brain’s grouping mechanisms. The gray squares at the middle right in the box on the opposite page, which are surrounded by black, appear darker than those on the middle left, which are enclosed by white.

This effect may occur because the gray elements on the right appear to lie in the same plane with the white background, rather than the black bars of the dungeon window. A reverse contrast illusion by University of Crete perception researcher Elias Economou makes the same point. The gray bar [see bottom right in box on opposite page], even though it is completely bordered by black, appears darker, apparently because it is a member of the group of white bars.

These fun illusions have a serious side. They show that the brain cannot compute the gray levels we perceive by simply comparing the luminances of two neighboring surfaces alone. Rather the surrounding context comes into play in a very sophisticated way. The fact that most people are

unaware of the difficulty of the problem testifies to the remarkable achievement of the human visual system.

The Big Picture

Scientific consensus on how the brain computes black and white remains further down the road. Current theories fall into three classes: low, middle and high level. Low-level theories, based on neural spatial-filtering mechanisms that encode local contrast, fail to predict the gray shades that people see. High-level theories treat the computation of surface gray shades as a kind of unconscious intellectual process in which the intensity of light illuminating a surface is automatically taken into account. Such processes might be intuitively appealing but tell us neither what to look for in the brain nor how to program a robot. Middle-level theories parse each scene into multiple frames of reference, each containing its own anchor. These theories specify the operations by which black, white and gray shades are computed better than the high-level theories do, while accounting for human perception of gray surfaces better than the low-level theories do.

But before we can truly comprehend this aspect of vision—or program a robot to do what our human system does—we will need a better understanding of how boundaries are processed. The human eye, like the robot, starts with a two-dimensional picture of the scene. How does it determine which regions of the picture should be grouped together and assigned a common anchor? Vision scientists will continue to propose hypotheses and test them with experiments. Step by step, we will force the visual system to give up its secrets.

Decoding human visual computing may be the best way to build robots that can see. But more important, it may be the best way to get a grip on how the brain works. **M**

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Inside the Mind of a Savant

Kim Peek—the inspiration for *Rain Man*—possesses one of the most extraordinary memories ever recorded. Until we can explain his abilities, we cannot pretend to understand human cognition

By Darold A. Treffert and Daniel D. Christensen

When J. Langdon Down first described savant syndrome in 1887, coining its name and noting its association with astounding powers of memory, he cited a patient who could recite Edward Gibbon's *The Decline and Fall of the Roman Empire* verbatim. Since then, in almost all cases, savant memory has been linked to a specific domain, such as music, art or mathematics. But phenomenal memory is itself the skill in a 54-year-old man named Kim Peek. His friends call him "Kim-puter."

He can, indeed, pull a fact from his mental library as fast as a search engine can mine the Internet. Peek began memorizing books at the age of 18 months, as they were read to him. He has learned 9,000 books by heart so far. He reads a page in eight to 10 seconds and places the memorized book upside down on the shelf to signify that it is now on his mental "hard drive."

Peek's memory extends to at least 15 interests—among them, world and American history, sports, movies, geography, space programs, actors and actresses, the Bible, church history, literature, Shakespeare and classical music. He knows all the area codes and zip codes in the U.S., together with the television stations serving those locales. He learns the maps in the front of phone books and can provide MapQuest-like travel directions within any major U.S. city or between any pair of them. He can identify hundreds of classical compositions, tell when and where each was composed and first performed, give the name of the composer and many biographical details, and even discuss the formal and tonal components of the music. Most intriguing of all, he appears to be developing a new skill in middle life. Whereas before he could merely talk about music, for the past two years he has been learning to play it.

It is an amazing feat in light of his severe developmental problems—characteristics shared, in varying extents, by all savants. He walks with a sidelong gait, cannot button his



Kim Peek stands in front
of an image of his brain.

Peek has memorized 9,000 books and can provide MapQuest-like directions between any major U.S. cities.

clothes, cannot manage the chores of daily life and has great difficulties with abstraction. Against these disabilities, his talents—which would be extraordinary in any person—shine all the brighter. An explanation of how Peek does what he does would provide better insight into why certain skills, including the ordinarily obscure skill of calendar calculating (always associated with massive memory), occur with such regularity among savants. Recently, when an interviewer offered that he had been born on March 31, 1956, Peek noted, in less than a second, that it was a Saturday on Easter weekend.

Imaging studies of Peek's brain thus far show considerable structural abnormality [see box on page 54]. These findings cannot yet be linked directly to any of his skills; that quest is just beginning. Newer imaging techniques that plot the brain's functions—rather than just its structure—should provide more insight, though. In the meantime, we believe it is worthwhile to document the remarkable things that Peek can do. People like him are not easily found, and savantism offers a unique window into the mind. If we cannot explain it, we cannot claim full understanding of how the brain functions.

An Unusual Brain

Peek was born on November 11, 1951. He had an enlarged head, on the back of which was an

encephalocele, or baseball-size “blister,” which spontaneously resolved. But there were also other brain abnormalities, including a malformed cerebellum. One of us (Christensen) did the initial MRI brain scans on Peek in 1988 and has followed his progress ever since.

The cerebellar findings may account for Peek's problems with coordination and mobility. But more striking still is the absence of a corpus callosum, the sizable stalk of nerve tissue that normally connects the left and right halves of the brain. We do not know what to make of this defect, because, although it is rare, it is not always accompanied by functional disorders. Some people lack the structure without suffering from any detectable problems at all. Yet in people whose corpus callosum has been severed in adulthood, generally in an effort to prevent epileptic seizures from spreading from one hemisphere to the other, a characteristic “split-brain” syndrome arises in which the estranged hemispheres begin to work almost independently of each other.

It would seem that those born without a corpus callosum somehow develop back channels of communication between the hemispheres. Perhaps the resulting structures allow the two hemispheres to function, in certain respects, as one giant hemisphere, putting normally separate functions under the same roof, as it were. If so, then Peek may owe some of his talents to this particular abnormality. In any case, the fact that some people lacking a corpus callosum suffer no disabilities, whereas others have savant abilities, makes its purpose less clear than formerly thought. Neurologists joke that its only two certain functions are to propagate seizures and hold the brain together.

Theory guides us in one respect. Peek's brain shows abnormalities in the left hemisphere, a pattern found in many savants. What is more, left hemisphere damage has been invoked as an explanation of why males are much more likely than females to display not only savantism but also dyslexia, stuttering, delayed speech, and autism. Also supporting the role of left hemisphere damage are the many reported cases of “acquired savant syndrome,” in which older children and adults suddenly develop savant skills after damage to the left hemisphere.

What does all this evidence imply? One possibility is that when the left hemisphere cannot

FAST FACTS

Peek's Peaks

1>> Savants possess great skills. Kim Peek cannot button his shirt but knows all U.S. zip codes and can recite music he heard only once 40 years ago.

2>> Peek's brain is missing a corpus callosum, which connects the hemispheres. This abnormality and others evoke a key question: In development, does the brain compensate for damage or does damage simply allow latent abilities to emerge?

3>> Rote learning eventually developed into associative thinking for Peek, with creativity that has helped him engage the wider world. A savant's skills should never be dismissed but should be cultivated for the person's intellectual and social advancement.

ETHAN HILL (preceding pages)

function properly, the right hemisphere compensates by developing new skills, perhaps by recruiting brain tissue normally earmarked for other purposes. Another possibility is that injury to the left hemisphere merely unveils skills that had been latent in the right hemisphere all along, a phenomenon some have called a release from the “tyranny” of the dominant left hemisphere.

Peek underwent psychological testing in 1988. His overall IQ score was 87, but the verbal and performance subtests varied greatly, with some scores falling in the superior range of intelligence and others in the mentally retarded range. The psychological report concluded, therefore, that “Kim’s IQ classification is not a valid description of his intellectual ability.” The “general intelligence” versus “multiple intelligences” debate rages on in psychology. We believe that Peek’s case argues for the latter point of view.

Peek’s overall diagnosis was “developmental disorder not otherwise specified,” with no diagnosis of autistic disorder. Indeed, although autism is more commonly linked with savantism than is any other single disorder, only about half of all savants are autistic. In contrast with autistic people, Peek is outgoing and quite personable. One thing that does seem necessary for the full development of savant skills is a strong interest in the subject matter in question.

Memory and Music

In Peek’s case, all the interests began in rote memorization but later progressed to something more. Although Peek generally has a limited capacity for abstract or conceptual thinking—he cannot, for example, explain many commonplace proverbs—he does comprehend much of the material he has committed to memory. This degree of comprehension is unusual among savants. Down himself coined the interesting phrase “verbal adhesion” to describe the savant’s ability to remember huge quantities of words without comprehension. Sarah Parker, a graduate student in psychology at the University of Pennsylvania, in a description of a savant named Gordon stated it more colorfully when she noted that “owning a kiln of bricks does not make one a mason.” Peek not only owns a large kiln of bricks, he has also become a strikingly creative and versatile word mason within his chosen areas of expertise.

Sometimes his answers are quite concrete and literal. Once when asked by his father in a restaurant to “lower his voice,” Peek merely slid lower into his chair, thus lowering his voice box. In other cases, his answers can seem quite ingenious. In



one of his talks he answered a question about Abraham Lincoln’s Gettysburg Address by responding, “Will’s house, 227 North West Front Street. But he stayed there only one night—he gave the speech the next day.” Peek intended no joke, but when his questioner laughed, he saw the point; since then, he has purposely recycled the story with humorous intent and effect.

Peek does have the power to make clever connections. He once attended a Shakespeare festival sponsored by a philanthropist known by the initials O.C., whose laryngitis threatened to keep him from acknowledging a testimonial. Peek—a fan of Shakespeare, and like him, an incorrigible punster—quipped, “O.C., can you say?”

Such creative use of material that had originally been memorized by rote can be seen as the verbal equivalent of a musician’s improvisation. Like the musician, Peek thinks quickly, so quickly that it can be difficult to keep up with his intri-

Peek reads a page in eight to 10 seconds, learning it by heart as he goes. His mental library of 9,000 books includes encyclopedic coverage of everything from Shakespeare to musical composers to the maps of all major U.S. cities.

(The Authors)

DAROLD A. TREFFERT and **DANIEL D. CHRISTENSEN** have long been fascinated by savantism. Treffert, a psychiatrist in Wisconsin, has done research on autism and savant syndrome since 1962, the year he first met a savant. He was consultant to the movie *Rain Man* and is author of *Extraordinary People: Understanding Savant Syndrome*. Christensen is clinical professor of psychiatry, clinical professor of neurology and adjunct professor of pharmacology at the University of Utah Medical School.

cate associations. Often he seems two or three steps ahead of his audiences in his responses.

A rather startling new dimension to Peek's savant skills has recently surfaced. In 2002 he met April Greenan, professor of music at the University of Utah. With her help, he soon began to play the piano and to enhance his discussion of compositions by playing passages from them, demonstrating on the keyboard many of the pieces he recalled from his massive mental library. Peek also has remarkable long-term memory of pitch, remembering the original pitch level of each composition.

He readily identifies the timbre of any instrumental passage. For example, he presented the

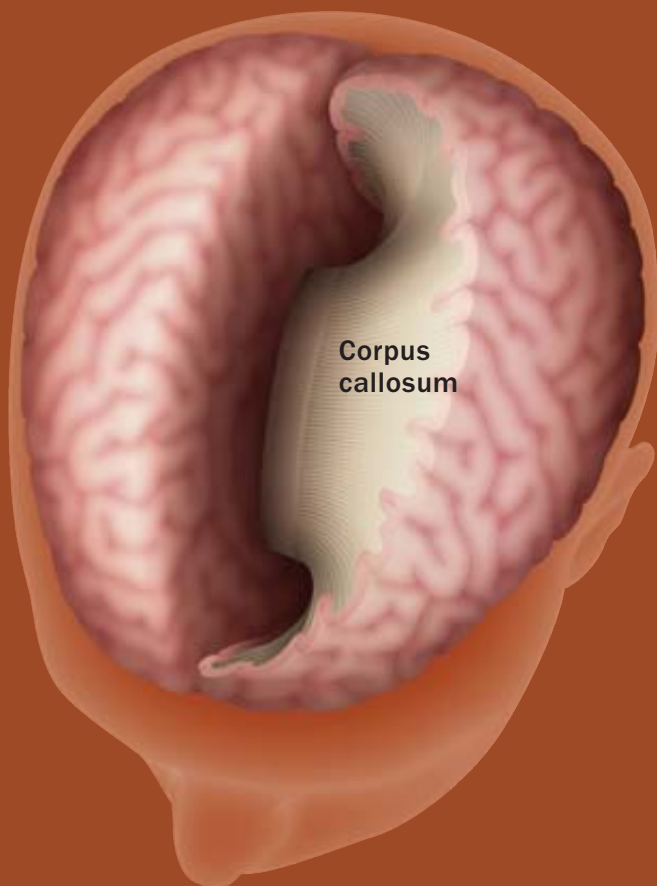
opening of Bedrich Smetana's orchestral tone poem *The Moldau* by reducing the flute and clarinet parts to an arpeggiated figure in his left hand on the piano. And he explained that the oboes and bassoons enter with the primary theme, which he then reduced to pitches played singly and then in thirds by his right hand (the left-hand figure continuing as it does in the score). His comprehension of musical styles is demonstrated in his ability to identify composers of pieces he had not previously heard by assessing the piece's musical style and deducing who that composer might be.

Though Peek is still physically awkward, his manual dexterity is increasing. When seated at the piano, he may play the piece he wishes to dis-

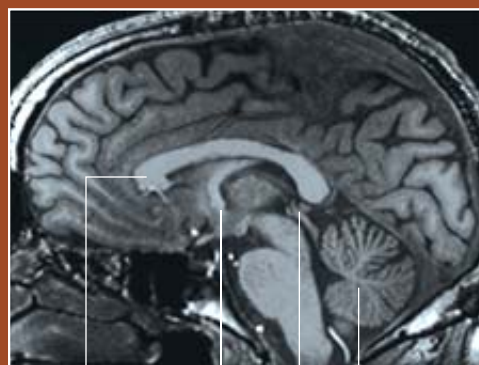
A Missing Connection?

Kim Peek's brain (*bottom right*) differs from typical brains (*diagram and top right*) in several ways. Peek's brain and head are very large, each in the 99th percentile. Most striking is the complete absence of the corpus callosum, which normally connects the left and right hemispheres. Missing, too, are the anterior and posterior

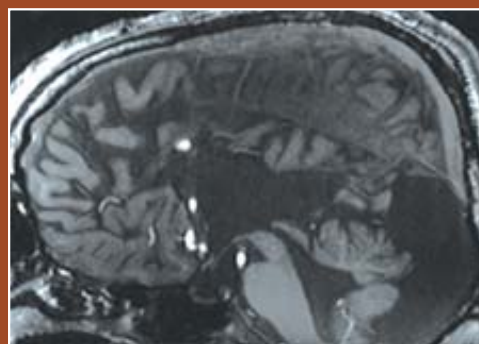
commissures, which also link the hemispheres. The cerebellum, responsible for certain motor functions, is smaller than usual and malformed, with fluid occupying much of the surrounding space; this may explain some of Peek's difficulties with coordination. What role these abnormalities play in his mental abilities is being investigated.



Normal brain



Kim Peek's brain



cuss, sing the passage of interest or describe the music verbally, shifting seamlessly from one mode to another. Peek pays attention to rhythm as well, lightly tapping the beat on his chest with his right hand or, when playing, tapping his right foot.

Greenan, a Mozart scholar, makes these observations: “Kim’s ability to recall every detail of a composition he has heard—in many cases only once and more than 40 years ago—is astonishing. The connections he draws between and weaves through compositions, composer’s lives, historical events, movie soundtracks and thousands of facts stored in his database reveal enormous intellectual capacity.” She even compares him to Mozart, who also had an enlarged head, a fascination with numbers and uneven social skills. She wonders whether Peek might even learn to compose.

Life after *Rain Man*

It is not surprising that Peek’s prodigious memory caught the attention of writer Barry Morrow at a chance meeting in 1984 and inspired him to write the screenplay for *Rain Man*, whose main character, Raymond Babbitt, is a savant played by Dustin Hoffman. The movie is purely fictional and does not tell Peek’s life story, even in outline. But in one remarkably prescient scene, Raymond instantly computes square roots in his head, and his brother, Charlie, remarks, “He ought to work for NASA or something.” For Peek, such a collaboration might well happen.

NASA has proposed to make a high-resolution 3-D anatomical model of Peek’s brain architecture. Richard Boyle, director of the NASA BioVIS Technology Center, describes the project as part of a larger effort to fuse image data from as wide a range of brains as possible. The data, both static and functional, should enable investigators to identify changes in the brain that accompany thought and behavior. NASA hopes that this detailed model will enable physicians to improve their ability to interpret output from far less capable ultrasound imaging systems, which are the only kind that can now be carried into space to monitor astronauts.

The filming of *Rain Man* and the movie’s subsequent success was a turning point in Peek’s life. Before then, he had been reclusive, retreating to his room when company came; afterward, the confidence he gained from his contacts with the filmmakers, together with the celebrity provided by the movie’s success, inspired him and his father, Fran Peek, to share Kim’s talents with many audiences. They became enthusiastic emissaries for people with disabilities, and they have shared their story with more than 2.6 million people.



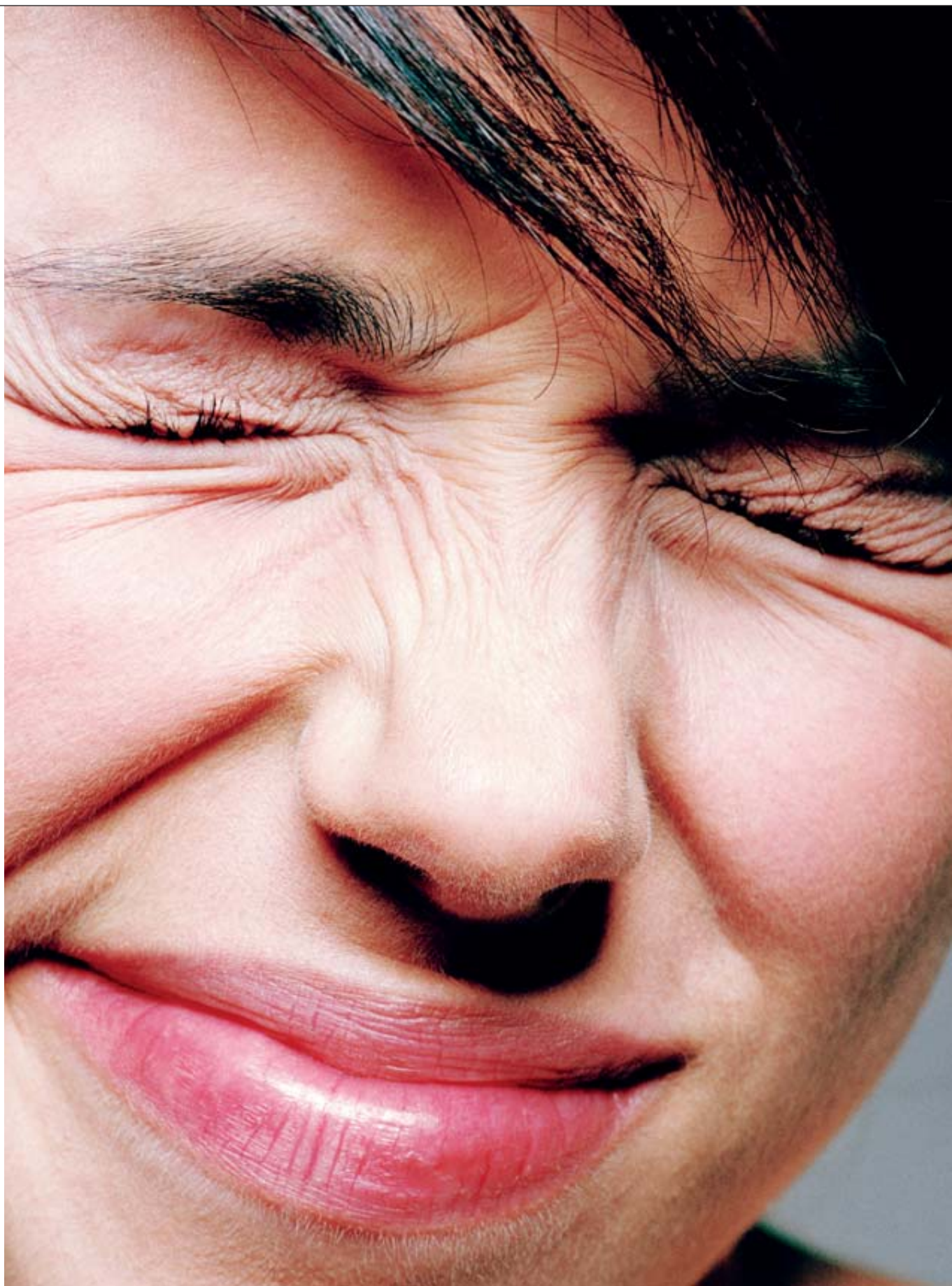
We believe that Peek’s transformation has general applicability. Much of what scientists know about health comes from the study of pathologies, and certainly much of what will be learned about normal memory will come from studying unusual memory. In the meantime, we draw some practical conclusions for the care of persons with special needs who have some savant skill. We recommend that family and other caregivers “train the talent,” rather than dismissing such skills as frivolous, as a means for the savant to connect with other people and mitigate the effects of the disability. It is not an easy path, because disability and limitations still require a great deal of dedication, patience and hard work—as Peek’s father, by his example, so convincingly demonstrates.

Further exploration of savant syndrome will provide both scientific insights and stories of immense human interest. Kim Peek provides ample evidence of both. **M**

Piano playing is Peek’s most recently acquired skill, one at which he is becoming increasingly adept despite having poor coordination. Music professor April Greenan (seated) and Peek’s father, Fran, have encouraged his efforts.

(Further Reading)

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- ◆ **Extraordinary People: Understanding Savant Syndrome.** Updated edition. Darold A. Treffert. iUniverse, Inc., 2006.
- ◆ **www.savantsyndrome.com**, a Web site maintained by the Wisconsin Medical Society.



SERGE KROUGLIKOFF Getty Images

BITTER COULD BE BETTER

New additives might fool the brain into thinking that bitter foods and medicines do not really taste that bad

By Stefanie Reinberger

Ashley grimaces. She really wants to spit out the vegetables she has just put in her mouth—they are horribly bitter. But politeness forbids. After all, the man from Cameroon and his wife have invited her to their home for dinner. And strangely, her hosts seem to be savoring the spinachlike *ndole*, a favorite from their homeland, which can be found in some specialty stores under the name “bitterleaf.”

That’s certainly the right name, Ashley has just discovered. But how can the experience be so different for her? Because the way individuals perceive flavors is determined not only by cultural familiarity but by molecular biology as well. Researchers are finding that genes activate very different sensitivities in each person’s set of taste buds. Ultimately these reactions are responsible for the “tastes” we perceive in our brains, especially bitterness. As scientists learn more, executives at food manufacturing companies are experimenting with special compounds that could cover up unpleasant flavors that turn some people off healthful foods. And

Savoring Cigarettes

Taste sensitivity might be added to nicotine metabolism and personality as a factor in why certain people smoke.

Researchers at the University of Wisconsin–Madison and the University of Utah examined 384 smokers and 183 nonsmokers, quantifying the activity of the subjects' gene that determines reaction to the bitter compound phenylthiocarbamide (PTC). They found that smokers who are less sensitive to bitter taste (known as nontasters) are more likely to rate taste as a strong reason for smoking. Smokers who are sensitive to bitterness (supertasters) were less likely to smoke for taste. Yet smokers who possessed a relatively uncommon variant of the PTC gene, which positions them as intermediate tasters, were far less likely to smoke for taste.

Psychiatry professor Dale Cannon of the University of Utah says the results, announced in February, indicate that genetic factors involving cigarette taste should be part of any analysis of nicotine dependence. More research is planned into why intermediate tasters are least drawn to tobacco's flavor.

—Mark Fischetti



pharmaceutical manufacturers are testing such bitter blockers to make a range of medicines more palatable.

Supertasters Provide a Clue

Scientific examination into our sense of taste began in earnest in 1931, after a mishap at a DuPont laboratory in Wilmington, Del. Chemist Arthur Fox had just synthesized a substance named phenylthiocarbamide (PTC) when the powdery material was swirled into the air by a gust of wind. His colleague, who got a bit of the powder in his mouth when he inhaled, complained about its awful pungency. Fox, however, did not experience any offensive sensation. He immediately tested his compound on other lab hands; some of them described PTC as mildly or extremely bitter, and others said it was tasteless.

About 60 years after Fox's incident, Linda Bartoshuk of Yale University determined that around 25 percent of men and women belong to the "PTC nontasters" group. Another 25 percent react intensely to both PTC and a related chemical called PROP (6-*n*-propylthiouracil). These

sensitive individuals respond more strongly to all four basic tastes—sweet, sour, salty and bitter. Investigators have also found that the same people are sensitive to the proposed fifth fundamental taste, "umami," demonstrated in recent years. (The term is a Japanese word, meaning "meaty and hearty," a sensation typical of high-protein foods.)

Studies of these supertasters in the past few years have elucidated how we taste and why the same food that is delectable to individuals such as Ashley can be delectable to her hosts. Painting a tongue with methylene blue dye stains most of it blue, leaving tiny pink dots—the taste papillae in which the taste buds reside. Although an average tongue contains 100 to 200 of the little knobs per square centimeter, supertasters may have twice as many, with individual papillae merging into one another. Nontasters have half the normal number of papillae, but each one is much larger. "Supertasters live in a neon taste world, and nontasters live in a pastel taste world," Bartoshuk says.

But the number of papillae only partly determines whether someone might want to spit out a bite of *ndole*. Which flavors we detect strongly, and how extreme they seem to us, depends above all on the molecular biology of our taste receptors. Some years ago researchers identified the

(The Author)

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CHRIS CRAYMER/Getty Images

first genes that code for bitter receptors, among them the ones that detect PTC and PROP. Soon thereafter, Un-Kyung Kim and his colleagues at the National Institute on Deafness and Other Communication Disorders discovered that several variants existed and were correlated with supertasters and nontasters.

Experts have since tried an assortment of techniques to further define our taste apparatus. Bernd Bufo and Wolfgang Meyerhof of the German Institute of Human Nutrition in Potsdam created an “artificial tongue”—a group of specially prepared taste bud cells in a petri dish. When the cells were stimulated with bitters, substances would be bound by the buds’ receptors and calcium levels inside the cells would rise, indicating the degree of perception.

Separate results from the Human Genome Project indicate that 25 genes are responsible for encoding receptors that detect bitter flavors, according to Bufo. Different receptor molecules detect different categories of substances. For example, the PTC/PROP receptor, known as TAS2R38, binds only to molecules related to PTC and PROP, which are found abundantly in broccoli, cabbage and other cruciferous plants. On the other hand, TAS2R16 specializes in the so-called glucopyranosides—which include substances that contain cyanide—such as those found in bitter almonds. Other receptors seem to be less selective, reacting to several classes of substances.

Bufo notes that because variations exist for all 25 bitter genes, scientists are now aware of 104 different receptor types for such compounds. Our sense of “bitter” is therefore highly refined and very individual.

Early-Warning System

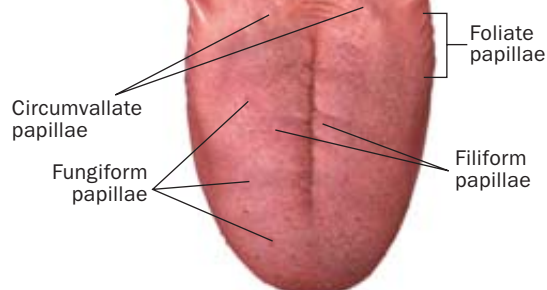
Our perception of bitterness is much more robust than it is for the other tastes. Some evolutionary biologists say that is because bitterness has long been a vital warning signal, causing us to immediately spit out anything that tastes horrible. For example, strychnine, found in plants belonging to the gentian family, activates such receptors. Early humans who better discriminated among acrid substances would have had a survival advantage as they continued to discover potential new foods.

In July 2005 Bufo and Nicole Soranzo of University College London published evidence for this thesis. They investigated the genetic variability of the TAS2R16 receptor among 997 people from 60 different parts of the world. The data showed that 98 percent of people outside of Af-

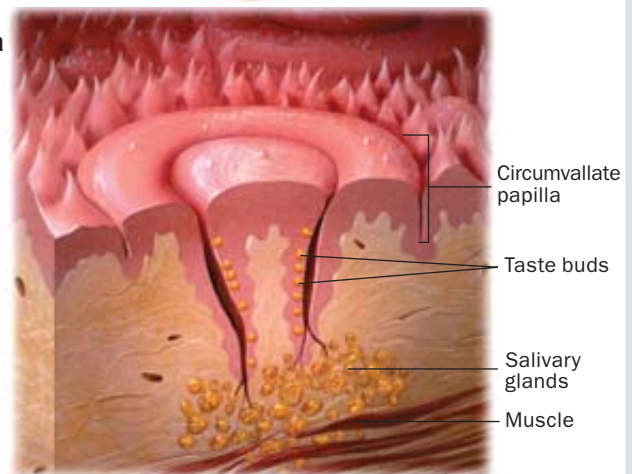
Taste Detector

On the tongue, various types of raised papillae contain taste buds, except for the filiform. Chemicals from food enter a taste bud’s pore and interact with microvilli, causing electrochemical changes in the taste cell that send nerve signals to the brain.

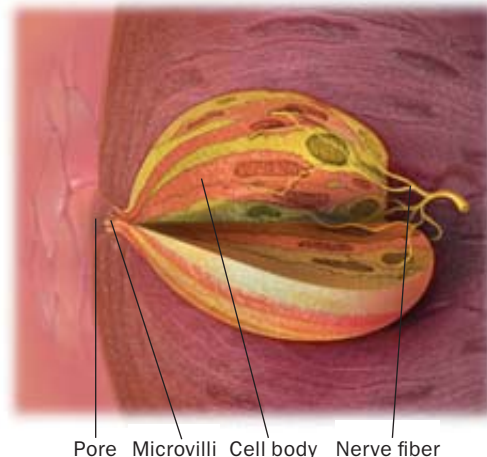
Tongue



Papilla



Taste bud



Our sense of bitterness is **highly individual**; we have 104 different receptors for such substances.

rica possess a version of the receptor that makes them extremely sensitive to the bitter substances in the glucopyranoside family. This genetic variant arose at least 80,000 years ago and possibly as long as 800,000 years ago.

A less sensitive, earlier version of the receptor was found among 14 percent of Africans. Did this variant represent the survivors of a population that remained after the more sensitive mutation arose? Perhaps. But Bufe and Soranzo offer another explanation: that less sensitive receptors would allow consumption of small amounts of substances containing cyanide, which, once metabolized, could in turn provide enhanced defense against malaria. Maps illustrate that most of the people who have the old receptor live precisely in regions where malaria is traditionally

most severe. Other genes conferring resistance to malaria are also widespread in the same areas.

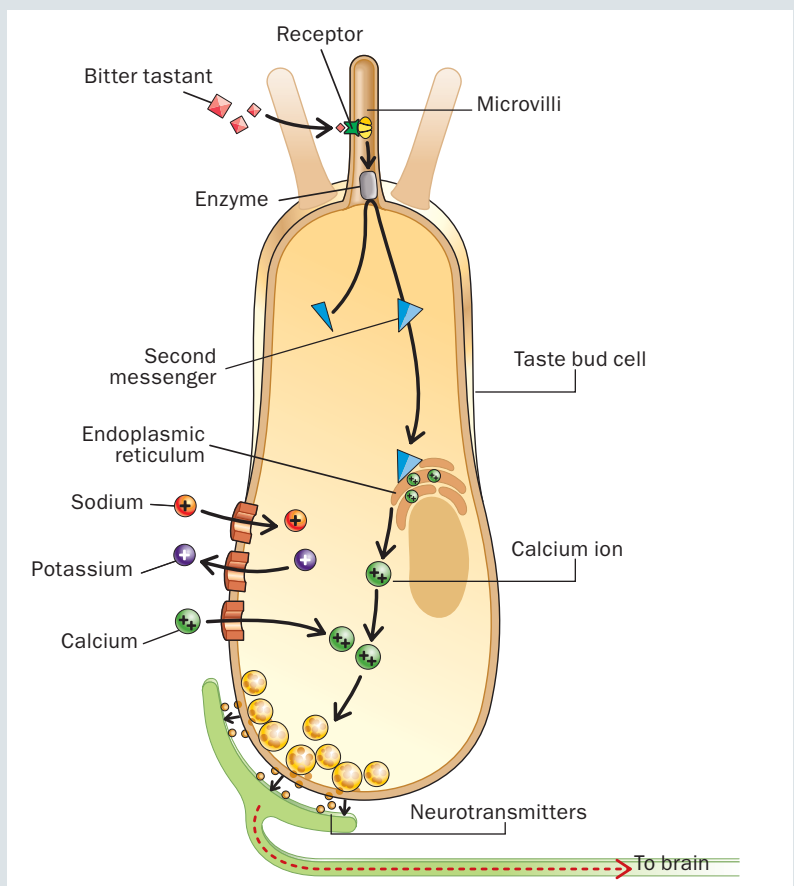
For everyone else, it is apparently an advantage to detect even small quantities of bitters. The glucopyranosides include substances that release toxic cyanide when metabolized, such as amygdalin in bitter almonds or linamarin in manioc. Even a single dose of one milligram of cyanide per kilogram of body weight is lethal for most mammals. A slight change in the genes for the TAS2R16 receptor must have had a significant influence on feeding behavior, survival chances and the spread of the human species.

Broccoli and Aspirin

What was useful to early *Homo sapiens* can be a problem for folks in the 21st century, how-

A Bitter Signal

Receptors that are on the microvilli of a taste cell spark enzymes to release second messengers, which in turn instruct the endoplasmic reticulum to discharge calcium ions. A calcium buildup causes the cell to fire neurotransmitters that notify the brain. Other food chemicals, such as sodium, may enter the cell directly (*left*).



JARED SCHNEIDMAN DESIGN

ever. People who are unusually sensitive to pungent substances often avoid nutritious vegetables such as broccoli because of their taste. Nutritionists want to know how much these choices affect the health of individuals and whether it would be advisable for such people to use custom food additives to improve taste and thus nutrition. Food manufacturers have vested interests, too; today they often add large quantities of sweeteners to products such as cola to override the bitterness of the caffeine. A bitter blocker could simply turn off consumers' relevant taste buds, and the products could be made and promoted as low in calories.

Linguagen Corporation, a small biotech firm in Cranbury, N.J., has already developed such a bitter blocker: adenosine monophosphate (AMP). The company says the nucleotide, which is produced naturally by the body and found in many living cells, suppresses the bitterness sensation without any side effects. AMP apparently does not act directly on taste bud receptors but seems to interfere with the signal from the taste cells to the nerve fibers that subsequently head toward the brain. Although Linguagen's researchers have not defined the mechanism exactly, technical director Richard McGregor says that company researchers believe AMP interacts with a molecule in the cell membrane to hinder signal transmission. Linguagen is searching for other blockers as well.

The U.S. Food and Drug Administration approved AMP in September 2004, but it remains to be seen if Linguagen's bitter blocker will succeed in commercial food production as it did in the lab. Some critics observe that the compound has a taste of its own, in the umami category, that is somewhat reminiscent of beef broth. That quality may make it undesirable for sweets or soda. Other skeptics are wary of bitter blockers on general terms. Widespread use could possibly undermine a natural, protective function; our tongue's receptors might become dulled to toxic substances or spoiled foods. Such additives might also make it easier for companies to manufacture and to market low-quality foods.

The pharmaceutical industry is equally interested in new substances that could mask unpleasant flavors. Our detectors react strongly to many medications. The TAS2R16 receptor often recoils from acetylsalicylic acid—the active ingredient in aspirin. Flavor-optimized drugs would be especially valuable for treating children, who often refuse to swallow nasty-tasting pills and syrups. And chronically ill people such as AIDS patients, who have to force down many unpleas-



ant tablets daily, would greatly appreciate more agreeable formulations.

McGregor points out that AMP is not strong enough to completely suppress the concentrated bitterness of many drugs, and he acknowledges that the substance alters a user's sense of taste for a range of chemicals—including the hops flavor of a microbrew drunk with dinner or the pleasant bite of dark chocolate for dessert. Finding more ideal bitter blockers—whether for drugs or delicacies—will therefore require further basic research. Bufo says precise structural analyses of bitter chemicals and where they bind to various receptors should lead to molecules that can temporarily blind our tongues to very specific substances in a particular drug or food, instead of blocking the detection of everything bitter. Many hours of work are still needed, however, before it becomes easier to swallow a bitter pill. **M**

Compounds that block bad tastes would make medicines easier to take.

(Further Reading)

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- ◆ **The Molecular Basis of Individual Differences in Phenylthiocarbamide and Propylthiouracil Bitterness Perception.** Bernd Bufo et al. in *Current Biology*, Vol. 15, No. 4, pages 322–327; February 22, 2005.

CONTROLLING EPILEPSY

ONE WOMAN'S JOURNEY THROUGH DIAGNOSIS AND TREATMENT SHOWS HOW FAR WE HAVE COME IN USING SURGERY TO DEFUSE SEIZURES BY CHRISTIAN HOPPE

Trudy, a 34-year-old bank employee, had been suffering from epilepsy for more than 18 years. She had tried all the usual medications, with little success. Typically she would feel nauseated before an oncoming seizure, then lose consciousness. A few minutes later she would wake up, exhausted. According to her husband, she would smack her lips during her seizures and fumble with her hands.

When it got to the point that Trudy was experiencing two to three seizures a week, she decided to contact the Epilepsy Clinic at Bonn University, Germany, which she had heard about in a television report. Several weeks later she had her first outpatient appointment. After a detailed discussion of her medical history, physicians took blood samples, an electroencephalogram (EEG) of her brain and magnetic resonance images (MRI) of her head. Within days a doctor called to tell Trudy that surgery was recommended and that she should come in for an inpatient workup. Trudy was glad—and scared.

More than 2.5 million people in the U.S. and 600,000 in Germany have epilepsy. About two thirds of them are freed of seizures with drug therapy, but for the rest, surgery is the only other option. Although the operations carry risks, 60 percent of adults and 70 percent of children remain free of seizures afterward. As physicians perform more procedures, the presurgical testing and the final outcomes are helping researchers learn more about the condition and the workings of the human brain.

Many Names

Seizures occur when groups of overexcited neurons suddenly fire in unusual synchrony. The chorus rings out from a limited region of the brain—the onset zone. Given Trudy's symptoms, the clinic's specialists suspected her seizures were initiated in the temporal lobe. Sure enough, radiologists reading the MRI scans detected peculiarities in the left hippocampus—a C-shaped structure deep within the temporal lobe—



Patients at the Epilepsy Clinic at Bonn University are monitored around the clock.



which seemed to have resulted from scarring. Back when Trudy experienced her first seizures, the minute structural changes would not have been visible; only since the debut of high-resolution MRI technology in the mid-1990s has such damage been discernible.

The “sacred disease” of the Greeks, Valentine’s sickness, falling sickness—the illness has afflicted human beings since time immemorial. During a

Exorcising the Demon

Our understanding of neuronal behavior during a seizure advanced markedly after 1924, when neuropsychiatrist Hans Berger developed electroencephalography. Electrodes affixed to the scalp register fluctuations in the electromagnetic fields created by neuronal activity. In modern instruments the signals are electronically enhanced, digitized and stored. It is impressive how an EEG

Surgeons drilled **two small holes** in Trudy’s cranium, then slipped a fine electrode into each temporal lobe.

seizure, the victim appears to be obeying an alien will. That is why epilepsy was often assumed to have supernatural causes. Followers of the ancient Tibetan Bon religion believed that epileptics were chosen people, but the ancient Jewish and later Christian traditions viewed the condition as God’s punishment or the work of demons. Not everyone was convinced, however. The legendary Greek physician Hippocrates observed in the fifth century B.C. that head injuries in soldiers and gladiators sometimes led to seizures that mimicked those of his own patients. He concluded that the brain caused the affliction, but scientific research did not make substantial gains until the 20th century.

Today physicians distinguish more than 30 forms of epilepsy. One of the best known is characterized by the petit mal seizure, sometimes called absence seizure—minor episodes of 10 to 20 seconds during which victims’ eyeballs may roll upward and they no longer respond to stimuli. A grand mal seizure has a generalized pattern whereby the person first loses consciousness, then becomes rigid, often falling. The arms and legs convulse and twitch uncontrollably, for as long as two minutes. At least half of all cases are symptomatic—attributed to abnormal changes in brain structure caused by tumors, trauma or inflammation. In other cases, however, no such peculiarities are detectable.

Neither a single nor several random seizures necessarily lead to epilepsy. High fever occasionally causes convulsions in infants, and sleep deprivation can trigger a seizure in children and teenagers. Approximately 10 percent of all people will experience at least one seizure during their lifetime. Our brains differ primarily in the partially genetic individual threshold for an episode, beyond which groups of neurons fire spontaneously and synchronously.

changes at the moment a grand mal seizure begins: just a second earlier the pens that trace activity on graph paper—like a seismograph—draw fine, mildly undulating lines. Suddenly, one electrode pen jumps. Then, within seconds, they all show the same sharp peaks and valleys, as thousands of neurons discharge in lockstep. It seems as if a neuronal bandleader suddenly gave the orchestra the direction, “All together now!”

The strong, rhythmic neuronal activity explains why the behavior and experience of the patient change so abruptly. The symptoms depend on where the epileptic onset zone, or “focus,” is located in the brain, how far the activity spreads from that focus, and what the involved brain areas normally do. One patient may barely notice a transient seizure, whereas another is plunged into violent, unconscious convulsions.

What determines when neurons will fire synchronously remains a riddle. Transitional phases, such as waking up, relaxing, or getting angry or stressed, appear to be precarious. Some people react to flickering light or acoustic stimuli. Sleep deprivation, physical exhaustion and alcohol all enhance the chance of seizures.

Patients understandably want to get rid of their epilepsy at all costs. Medication is the method of choice, and there are a dozen approved substances. Several new anticonvulsants (also known as antiepileptics) are in clinical trials. Yet all anticonvulsants have a drawback: they do not actually cure the cause. They only suppress the neuronal hyperactivity, thereby preventing seizures. Patients must therefore take these tablets every day. The drugs also have mild to severe side effects, including weight changes, fatigue and concentration problems.

Two primary surgical strategies exist: resection and transection. In resection, surgeons attempt to

Finding the Zone

Neuropsychologists at the Epilepsy Clinic at Bonn University test the cognitive performance of each candidate for epilepsy surgery in exams that last several hours. Overall intelligence, attention, working memory, verbal and nonverbal memory, speech, motor coordination and visual-constructive capacities (*shown in photograph*) are all assessed. Frequently, cognitive deficits correlate with the location of the seizure onset zone. For example, impaired declarative memory is the main problem facing many patients with temporal lobe epilepsy. Individuals with frontal lobe epilepsy often have trouble with strategic thinking or act impulsively. Candidates are also often placed in a functional MRI scanner, where they answer linguistic questions to identify brain regions involved in speech



processing. Cognitive testing is repeated one year after surgery. Usually the effects of removing brain tissue are surprisingly small, which is why epilepsy surgery is now generally viewed as a safe procedure. —C.H.

remove all of the onset region, but only that region. The prerequisite, naturally, is that there be a single onset zone that can be precisely localized. If this is not the case, then transection is done, to disconnect distant tracts of neurons that seem to fire together. Although this procedure does not lessen the frequency of seizures, it prevents their spread, minimizing the intensity of symptoms.

A third treatment, approved by the U.S. Food and Drug Administration in 1997, is vagus nerve stimulation. An impulse generator, much like a cardiac pacemaker, is implanted in the chest wall. It emits electrical signals that stimulate the vagus nerve in the left side of the neck. For some patients, this action reduces hyperreactivity in the brain after a few months, by a mechanism that researchers have not yet elucidated. Fewer than 5 percent of patients enjoy complete freedom from subsequent seizures, however.

Probing the Onset Zone

The current therapeutic rule of thumb is that if a patient continues to experience seizures after trying several medications for two to three years, he or she should be evaluated for surgery. Too many patients, or their doctors, wait too long, unnecessarily prolonging a fractured quality of life, as Trudy had. Soon after her initial outpatient exams, Trudy returned to the Bonn clinic for her inpatient stay.

Neuropsychologists first performed a variety

of mental tests [*see box above*]. Like many patients with temporal lobe epilepsy, Trudy apparently suffered from slight verbal memory impairment, which is known to occur more frequently when the seizure onset zone is in the left hippocampus. But whether her seizures truly originated there could be determined only during an actual seizure recorded by an EEG.

So Trudy checked into her private room at the center's monitoring unit, which trains video cameras on its guests 24 hours a day [*see illustration on pages 62 and 63*]. She wore a bonnet that held electrodes against her scalp, wired to a bedside EEG machine. Technicians who monitor the video in a separate room spring into action as soon as they notice telltale peculiarities that signify an oncoming seizure. When this occurs, they help patients and conduct short behavioral tests during the episode, which enable them to characterize the seizure more precisely.

Trudy did not have to wait long. Her first seizure ignited after only six hours. Three more followed in the first two days. Nevertheless, the electrode tracings did not enable physicians to locate the onset zone precisely; they could not tell

(The Author)

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The consequences of brain surgery can be simulated in advance by stimulating the cortex with implanted electrodes. A nurse asks the patient to perform various movements, to count, and to report on unusual sensations (*right*). Outside the room, technicians record how stimulation of brain regions affects perceptions and behavior (*left*).



conclusively whether the spark occurred in the left or right hippocampus. For some patients, the EEG signals become too distorted or damped as they travel through the brain tissue and skull. Better accuracy would require that electrodes be implanted under the cranium.

Without hesitation, Trudy decided to undergo the procedure. Surgeons drilled two small holes in the cranium, above the left and right temporal lobes, and placed electrodes almost directly on the cerebral cortex. They then carefully slipped in a fine electrode at a precalculated angle from the occipital lobe deep into both the right and left temporal lobes, to measure activity along the length of the amygdala at the core of the brain all the way to the hippocampus.

Two days later Trudy had two seizures identical to the previous ones. Each time, the epileptic activity began deep within the area by the left electrode. All findings pointed to the left hippocampus as the sole onset zone. Trudy was a good candidate for epilepsy surgery.

Limiting Risk

The surgeons explained to Trudy that she was lucky the onset zone was limited to the hippocampus in one hemisphere. Under no circumstances can both hippocampi be removed. They told her about the famous case of an epileptic man known as H.M. at the Montreal Neurological Institute who had both hippocampi removed in 1953. Although the 27-year-old patient became largely free of seizures, the procedure robbed him of his memory. H.M. could access memories that had been stored prior to the op-

eration, but he forgot every subsequent experience within five minutes. At least one functional hippocampus is indispensable for our ability to “write” our ongoing autobiography.

Epilepsy patients from H.M.’s era through today have supplied scientists with important knowledge. The implanted electrodes offer a unique opportunity to measure brain activity in real time directly—something that even functional MRI cannot do, because the images lag the actual processes by several seconds. Like many patients do, Trudy had consented to undergo a few experiments while the electrodes were in her head. She performed computerized exercises for 30 to 40 minutes, and the data showed precisely what brain activity correlated with a particular cognitive event, such as recognizing a word when it appeared on the computer screen. Based on such experiments, the Bonn researchers have since explained which brain regions are involved, and in what order, when we perceive a word, as well as when we later recall that word—a possible boon to understanding language impairments.

To minimize the risk of neurological damage, neurosurgeons remove as little brain tissue as possible. Today no one would resect two thirds of the temporal lobe, the way doctors did years ago. Much more common is to limit removal to the amygdala and hippocampus on one side, leaving the rest of that hemisphere’s temporal lobe untouched. The Bonn doctors recommended this form of surgery for Trudy.

Such standardized surgical routines have been worked out for many types of epilepsy. But if the onset zone is located in the frontal lobe or

the parietal lobe, it is hard to predict whether the operation will damage regions crucial to motor functions and speech, among other abilities. In these cases, doctors implant electrodes during the presurgical diagnostic workup. The electrodes record epileptic brain activity but also allow surgeons to apply electrical impulses to specific brain tissue. This procedure essentially sim-

Before surgery, Trudy had agreed that tissue taken from her brain could be used for research. Once extracted, it was immediately placed in a nutrient solution so electrophysiologists could test it even after 20 to 30 hours; most work would occur right away, though, given this chance to investigate living neurons that only a short time earlier had performed real functions in a human

Trudy consented to experiments, a boon to research on speech deficits and emotions.

ulates the consequences of the planned surgery. A neurologist will systematically activate each electrode with currents of various strengths and frequencies, while asking the patient to perform certain actions, such as counting out loud.

Stimulating a motor area might cause a patient's finger to start to twitch, for example, whereas pulsing the association cortex usually leads to speech deficits. More uncommon phenomena may occur, such as intense emotions or a sudden flashback to a long-lost memory. In one well-known case a woman began laughing hysterically, telling the doctors they were just too comical, the way they were standing around her. Changes in visual and spatial perception can also be fascinating. One patient, whose neurologists were examining the gyrus angularis in the parietal lobe, suddenly felt as if she were floating above the bed, observing herself lying there—an out-of-body experience. Her response indicates that, perhaps, “supernatural” experiences stem from odd brain processes.

The main purpose of such stimulation, before surgery, is to create a functional map of the individual's brain that will guide surgeons as they decide what and how much tissue to cut or remove.

Surgery Day

Trudy's surgery date finally arrived. The neurosurgeons needed half an hour to work through the large fissure that separates the temporal lobe from the frontal lobe and reach deep into the left temporal lobe. They were guided by MRI pictures of Trudy's brain and a microscope that enlarges the view of the surgical field. It is important to damage as few blood vessels as possible and to exert minimal pressure on the tissue. The next step was to carefully remove the amygdala and hippocampus in the left hemisphere. The operation took four hours.

brain. The researchers hoped to gain insight into what causes synchronized firing among thousands of neurons.

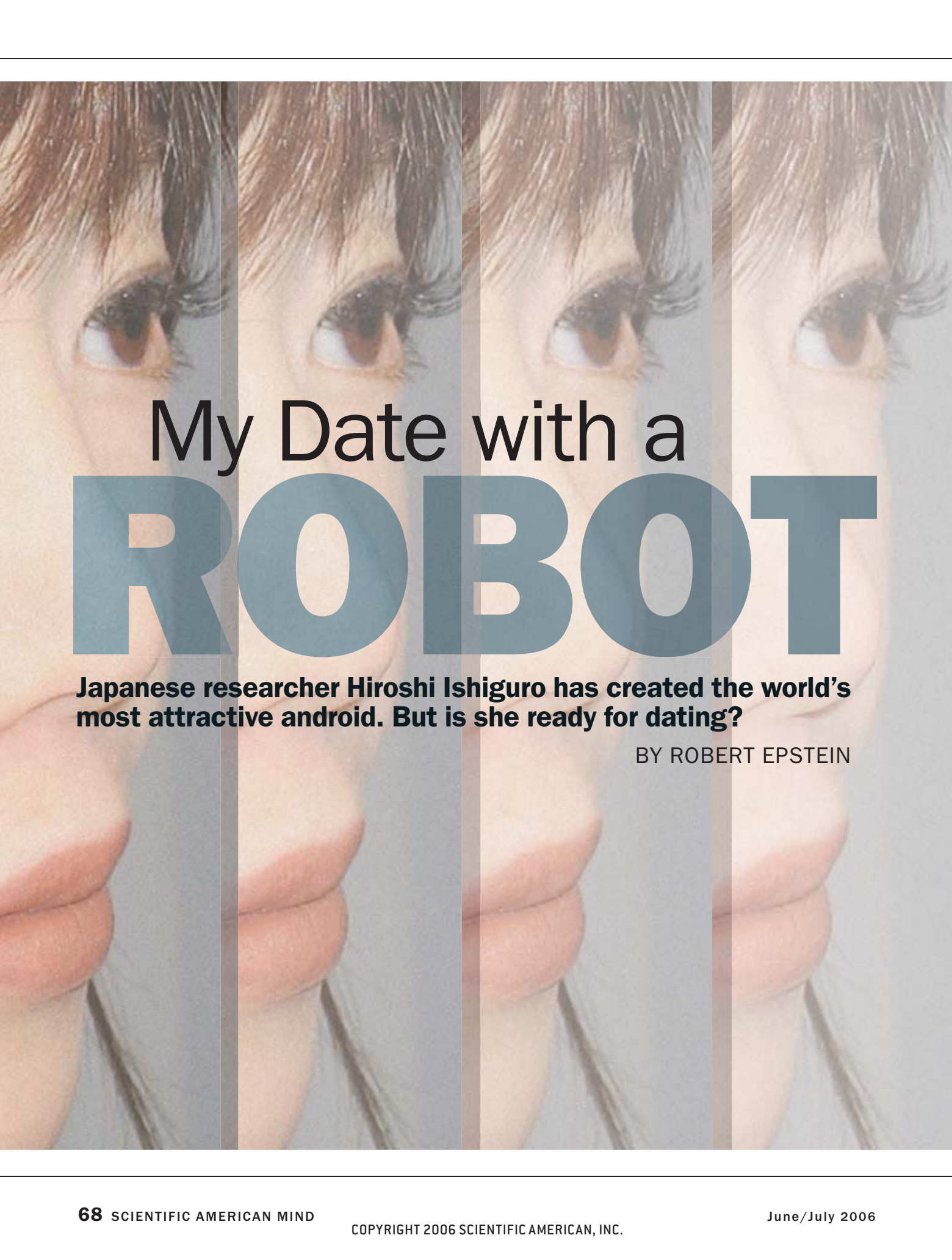
What the neuropathologists found was a markedly reduced number of nerve cells in certain lower hippocampus regions, confirming the suspected scarring. They also discovered a peculiarity in individual nerve cells: a larger than normal proportion spontaneously exhibited so-called burst discharges—the firing of three action potentials in uncommonly rapid succession. This propensity to discharge could have a number of causes, such as changes in ion channels or neurotransmitter receptors in the cell membrane. Such peculiarities may result from injury or be genetic.

Trudy recovered quickly from the operation. Her seizures, initially, seem to have stopped, and she is delighted. Still, she knows that the verbal memory deficits she already had—because of too many years of inadequate treatment—could worsen. More time will be needed to assess permanent changes, good and bad. But Trudy is optimistic. Her personal and work lives should be easier. And she will be less likely to be socially shunned, as if she were cursed.

The rest of us owe a debt of thanks to epilepsy patients such as Trudy who, during their own anxious medical ordeals, unselfishly participate in studies that help scientists—and ultimately all of us—better understand the human brain. The best thank-you society could offer in return would be greater understanding and acceptance of people suffering from this condition. **M**

(Further Reading)

- ◆ **Molecular and Cellular Mechanisms of Pharmacoresistance in Epilepsy.** Stefan Remy and Heinz Beck in *Brain*, Vol. 129, No. 1, pages 18–35; January 2006.
- ◆ The Epilepsy Foundation, www.epilepsyfoundation.org/epilepsyusa/, has a wide range of articles and patient information.



My Date with a **ROBOT**

Japanese researcher Hiroshi Ishiguro has created the world's most attractive android. But is she ready for dating?

BY ROBERT EPSTEIN



Hiroshi Ishiguro, Repliee Q1_{expo} and Robert Epstein.

I will never forget my first encounter with Eliza.



“My father just doesn’t appreciate me,” I keyed into a clunky, noisy teletype back in 1969. Eliza, a computer program that simulated a conversation with a Rogerian psychotherapist, responded, just as noisily, “Tell me more about your parents.” I responded, “Well, they just don’t GET it—you know, who I really am and what I’m capable of.” Eliza typed back, “Not being understood must be very hard for you.”

It was a dream come true, really, and it foretold that something big was right around the corner. The dream was that of the brilliant English mathematician Alan Turing, a developer of the modern concept of computing. In 1950, in an essay called “Computing Machinery and Intelligence,” Turing suggested that by the year 2000, computers would be powerful enough to “converse” with people—and even to fool most “average interrogator[s]” into thinking they were actually human, at least for five minutes or so.

JENNIFER BRAUN



Created by Joseph Weizenbaum of the Massachusetts Institute of Technology in the late 1960s, the extraordinary computer program Eliza seemed to suggest that Turing was not only right but that the so-called Turing Test would be passed well before the year 2000. I thought that we would have a winner by 1970.

But that's not what happened.

The Engine That Wouldn't

Eliza worked pretty well mainly because Weizenbaum picked a relatively easy task for it to handle. By definition, Rogerian therapists often say little on their own; they mainly “reflect” back whatever the client is saying. All the program had to do was to look for key words like “father” or “mother” and then offer a family-relevant reply (“Tell me more about your family”).

Real people are infinitely more capable. We know thousands of words and facts, we understand sentences we have never heard before, and almost everything we say is new in some sense. To pass the Turing Test, the thinking part of a computer program, often called the “engine,” would probably have to be every bit as sophisticated as the human brain, with its 100 billion neurons and 100 trillion connections.

In 1990 Weizenbaum and I served on a committee that oversaw the implementation of the Loebner Prize Competition—the first real Turing Test, pitting computer programs against “confederates” (hidden humans), all trying to convince judges of their humanness. So far, though, no software has fooled a judge for more than a few minutes. The Loebner competition is still held annually, and progress is still painfully slow. But one thing is certain: whereas the confederates in the competition will never get any smarter, the computers will.

Turing insisted that intelligence in a machine could be demonstrated by teletype—no visual cues were necessary. [For more on Turing and artificial intelligence, see “Electric Thoughts?” by Yvonne Raley; *SCIENTIFIC AMERICAN MIND*, April/May.] But it is inevitable that we will someday marry a host of emerging technologies to create an intelligent entity that has it all: the body, the mannerisms *and* the intellect.

My Cyborg Date

Having been obsessed with these issues for a long time, I was intrigued when I saw a BBC report about an extraordinary android that was demonstrated recently at a high-tech exposition in Japan. Created by computer scientist Hiroshi

JENNIFER BRAUN

(As I stood near her, I continued to feel those butterflies.) Repliee is **no mannequin**.

Ishiguro of Osaka University, it was said to be the most humanlike android ever built—and also quite attractive. How could I stay away?

Appropriate introductions having been made, the date was set. I put on my Sunday best—and my thinking cap, of course—and entered Ishiguro's laboratory with butterflies in my stomach. And, no, I am not kidding about that. I really was nervous, in part because I was getting a glimpse of the future and in part because I would be visiting a lovely humanlike female.

Unfortunately, before introducing me to Repliee Q1_{expo}, Ishiguro insisted on giving me a thorough rundown on his research activities, complete with PowerPoint presentation. Then he showed me robots that could navigate through mazes, guided by remote 360-degree cameras he had invented. Then he brought me to a dusty room where an old android had been discarded, which turned out to be—good grief!—a perfect replica of his four-year-old daughter. (This was getting creepy.)

Finally, the magic moment. There she was, dressed simply and demurely in gray slacks and a dark gray sweater buttoned nearly to the top. Her face, modeled after that of a local TV host, was indeed beautiful—and utterly realistic down to the smallest blemish. She was much better looking than in her photographs, but it is in another respect that snapshots of Repliee simply cannot do her justice. Her humanness, as Ishiguro's research shows, has as much to do with her movements as with her appearance. And, indeed, she blinks, her eyes dart around, her head shifts, her mouth twitches and sometimes she even smiles. With the help of sensors placed around the room, she also reacts to sound and movement.

On the down side, her silicone skin is not quite as pliable as a person's, and it is cold, pure and simple (there goes the urge for kissing). Ishiguro also revealed that as the silicone skin dries out over a year or two, it shrinks, causing, among other things, the eyes to bug out. (This contraction had already happened to the replica of Ishiguro's daughter.)

Her movement is also limited. She can only sit. She cannot walk. And although her lips move, Repliee can recite only prerecorded messages—no intelligent engine here. Still, I found something compellingly human about her. Our interaction



was superficial—typical of first dates—but as I stood near her, I continued to feel those butterflies; Repliee is no mannequin. Ishiguro is right about the powerful effect of subtle movement on the perception of humanness.

Ishiguro's next android? A perfect replica of the human he knows best: himself.

(The Author)

ROBERT EPSTEIN, who earned his Ph.D. in psychology at Harvard University in 1981, is the West Coast editor and former editor in chief of *Psychology Today*, a visiting scholar at the University of California, San Diego, and the founder and director emeritus of the Cambridge Center for Behavioral Studies in Concord, Mass. A longtime researcher and professor, he is co-editor (with Gary Roberts and Grace Beber) of a book that will be published next year by Kluwer Academic Publishers called *The Turing Test Sourcebook: Philosophical and Methodological Issues in the Quest for the Thinking Computer*.



A Conversation with Hiroshi Ishiguro

Epstein: Why create a robot that looks and moves so much like a human?

Ishiguro: For communication. We use our bodies to exchange various pieces of information.

Epstein: Right. I'm nodding my head, for example, when you speak. But we don't always need to see a body to communicate. We can communicate on the phone or by e-mail, for example.

Ishiguro: People prefer to communicate face to face—especially children and the elderly. So humanoid robots are highly desirable. But we are very sensitive both to the robot's appearance and its behavior. If either is incorrect in some way, people find that disturbing.

Epstein: When did you start building your androids, and who supports your work?

Ishiguro: I started three or four years ago, and the work is collaborative with the [Tokyo-based] Kokoro dinosaurs company. This is a small but famous company that makes big computer-controlled dinosaurs for natural history museums

around the world. The company knows how to use silicone and how to simulate natural behavior.

Epstein: Her blinking is very natural.

Ishiguro: Yes. Actually some elderly people and some children do not realize this is a robot.

Epstein: You have suggested that an android could be considered to be a kind of computer interface.

Ishiguro: Exactly. The keyboard and monitor are primitive. My brain was not designed to watch a display, and my fingers were not designed to type on a keyboard. My body is best suited for communicating with humans. The ideal medium for communicating with a computer is a humanoid robot, which is, of course, basically a computer with a humanlike interface.

Epstein: I know your first android was a replica of your daughter. How did that work out?

Ishiguro: Yes, my daughter was four years old at that time. But the replica's body was too small to fit all of the actuators we needed, so Repliee Q1_{expo}, the new android, is larger.

Epstein: You modeled your new android after a news reporter, Ayako Fujii. Was she pleased?

Ishiguro: Yes. In Japan, you see, we like our newscasters to be very young. When national newscasters are no longer young enough, they are shifted to local television. This particular newscaster was very famous, but she had been shifted to local television in Osaka. After she accepted my offer to appear in the World Expo as an android, she became very famous again.

Epstein: How perfect is the copy?

Ishiguro: To make a copy of a human, we use 3-D scanning and advanced technologies, but the most important thing is the texture of the skin. We reconstruct very detailed skin textures.

Epstein: Is the silicone painted?

Ishiguro: Yes. And the eyes are perfect copies—even with the blood vessels.

Epstein: Are you worried about the “uncanny valley”?

Ishiguro's daughter was the model for his first android.



TIM HORNIAK (top); EVERETT KENNEDY BROWN EPA/Landov (bottom)

Ishiguro: Oh, yes. When my daughter first saw her android, she started to cry. As Professor Masahiro Mori suggested in a famous article in 1970, when a robot is dissimilar to a human, its appearance is not disturbing. But when its appearance is close to that of a human—but not close enough—its appearance can become very disturbing, as if we are looking at a moving corpse. He called this effect the “uncanny valley”—the dramatic dip in the comfort curve.

A colleague and I have found another uncanny valley—one that occurs as a function of age. Very young children weren’t disturbed by our android, but with children three or four years old, the reactions were very bad. By the time people were 20, the reactions were good again. Very young children weren’t disturbed, we think, because they have not yet built a clear cognitive model of humanness.

Epstein: How do you avoid the uncanny valley problem?

Ishiguro: Just improve the appearance and the behaviors. With my daughter’s android, we had eight motors in the head but none in the body. Therefore, the motion and the behaviors were unsettling. When the performance improves, people are comfortable again and the details—such as skin texture and color—are very important. For Repliee, the makeup was applied by the newscaster’s own makeup artist, so the makeup is identical. But the new android’s body, it turns out, is still too small to put in all the actuators we need to create natural movement—especially in the chest and arms—so our next android will be male. In fact, it will be me. And when my android is done, I’m never coming back to the university.

Epstein: Maybe you should use Arnold Schwarzenegger’s body. More space.

Ishiguro: [Laughs]

Epstein: As perfect as her eyes are, they still seem a bit unsettling, perhaps because they lack the small, rapid movements of normal eyes.

Ishiguro: That’s because we’re using actuators, and they’re just not quick enough. In the next version, we’ll use small DC motors, but the problem with those is the noise.

Epstein: And you have performed a kind of Turing test with the android, have you not? What happened?



Ayako Fujii and android Repliee.

Ishiguro: We gave people two-second glimpses of the android, either when she was completely still or when she was moving in subtle ways. Without the movement, 70 percent of subjects said she was not human. With the movement, 70 percent said she was human. Now we need to consider how to extend this time period. Maybe, as you said, with small eye movements or perhaps other behaviors. In a sense, by learning how to make a perfect android, we are finding out precisely what it means to be *human*.

Epstein: Can you make a copy for me to take home to the U.S.?

Ishiguro: Yes, for about \$300,000. But that doesn’t include the connections and computers, so she won’t do anything.

Epstein: Forget it!

Epstein: How fast can this technology grow? When will we have the perfect android?

Ishiguro: For specialized applications, we might have sophisticated androids in 30 years or so, but I doubt that an android could ever be a spouse—well, maybe in 100 years. Perhaps someday robots will be better than humans in some respects, but still I believe that robots will never be completely human. They may want to be, like Mr. Data in *Star Trek*, but they will always lack some humanness. **M**

(Further Reading)

- ◆ Footage of Repliee is available at <http://androidvideo.com>
- ◆ **The Age of Spiritual Machines.** Ray Kurzweil. Penguin, 2000.
- ◆ **Alan Turing: The Enigma.** Andrew Hodges and Douglas Hofstadter. Walker and Company, 2000.
- ◆ **Build Your Own Humanoid Robots: Six Amazing and Affordable Projects.** Karl Williams. McGraw-Hill, 2004.

CIRCUIT TRAINING

Computer games for mental workouts

By Kaspar Mossman

“Your brain is in its 60s,”

Ryuta Kawashima announced. The disembodied head of the neuroscientist from Tohoku University in Japan wagged on the Nintendo screen and admonished: “If your brain is older than you, you should take note!”

Miffed, this 34-year-old biophysics Ph.D. candidate decided to do something about it. I would train my brain daily.

GETTY IMAGES



With many studies emphasizing the benefits of mental exercise for cognitive health, I knew I was not alone in my quest for a sharper mind. A 2002 federally funded study published in the *Journal of the American Medical Association*, for one, found that regular practice improved reasoning and memory in older adults. And, given the number of electronic puzzles and games arriving regularly on the market, companies are more than willing to help. To date, Nintendo has sold more than five million copies of brain games in Japan alone.

But what are they like to use? To find out, I decided to try out three new releases—all of

When FedEx delivered my advance copy, I eagerly jammed in the cartridge. Kawashima's visage appeared on the left screen, guiding me through a preliminary brain checkup: a "Stroop test." I was presented with the words "black," "blue," "red" and "yellow" in those colors—except that "black" was sometimes red and "yellow" was blue. (When you try to combine a routine, "automated" task, such as recognizing a color, with one that demands conscious attention, such as being able to name the word as "red" even if the type is "black," the result is "interference," or the Stroop effect. The phe-

“Hmm,” Kawashima mused. “Your brain seems to be **a little tired**, doesn't it?”

which tout themselves as having been designed with the aid of scientists: Nintendo's Brain Age, Learning Enhancement Corporation's BrainWare Safari, and CyberLearning Technology's Smart BrainGames.

Let the Games Begin

Nintendo, king of thumb-reflex games such as Mario Bros., has long targeted teenagers who have the speed of a mongoose. But this April, Nintendo unveiled Brain Age, a nifty game for adults that more reasonably requires only that we scribble with a plastic stylus. Brain Age (\$19.99; Nintendo DS controller, \$129.99) is the American cousin of Brain Training, which rocketed to popularity in Japan in 2005.

Brain Training was the brainchild of Kawashima, professor of neuroscience at Tohoku. His concept: your brain has an age of its own, independent of your body. If you do not use it, it gets old; if you do, it gets younger. The object of the game is to get your own brain age as low as possible. The ultimate goal is a brain age of 20. (Presumably people did not like being told they had the mind of a 13-year-old.) The controller calculates your score on various games and places you on a curve Kawashima obtained from testing real people aged 20 to 70.

The controller folds out to resemble the dashboard of a small spaceship. To play Brain Age, however, you turn it sideways so it resembles a book. The touch-sensitive screen recognizes nearly illegible handwriting. As you write, speakers produce a pleasing raspy sound, as of a quill pen on parchment.

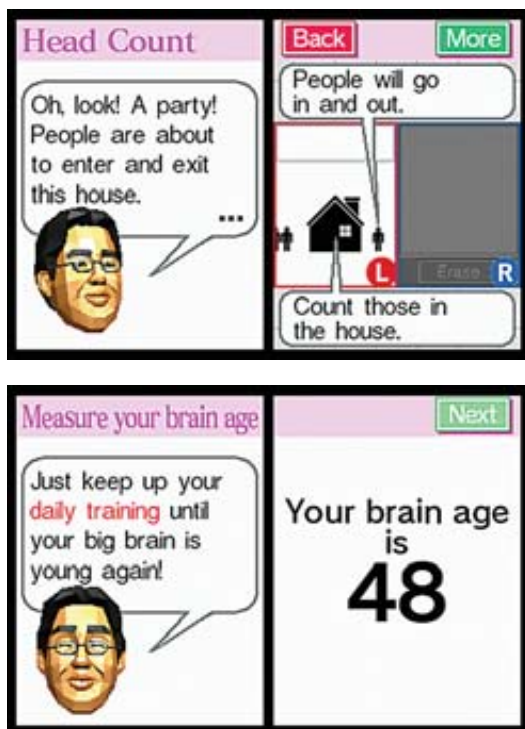
nomenon was first observed in the 1930s by John Ridley Stroop.) As instructed, I spoke the words aloud, careful not to let the colors distract me. The controller interpreted my voice.

After I got the irritating news that my brain was at an age when many people are contemplating retirement, I progressed to daily training: quick arithmetic, reading aloud from classic books (Kawashima trusts you to be honest about when you turn the page), picking numbers out of a cloud of twirling, sliding decoys.

After what I thought was an awesome performance, Kawashima declared that my brain age was 51. "This is a wake-up call! I fear your brain is asking you for help!" Furious, I raced through the math exercises, glared at the lists of words for memorization, and counted numbers until my frontal lobes began to radiate heat through my forehead. "Hmm," Kawashima mused. "Your brain seems to be a little tired, doesn't it?"

It sure was the next morning. I had made the mistake of training my brain late at night and had set my cranium buzzing so fast it would not let me sleep. Over the next week, I practiced hard (in the mornings) and worked my brain age down. Of course, as with any video game, once I learned certain tricks, which had nothing to do with intelligence, my score improved. During an activity called Calculations $\times 100$, for example, as the problems scrolled up the screen, I found I could look ahead and solve the next problem as my hand automatically wrote the previous answer.

On the third day Kawashima surprised me. "Draw a giraffe," he ordered. Then: "Africa." Next, to humiliate me, he showed me a real gi-



raffe and a real map of Africa. “Drawing objects from memory activates your prefrontal cortex!” As my scores improved, I was able to unlock new and more interesting games. Brain Age also allows multiple users; my fiancée insisted on playing, and we competed. She is a veterinarian and draws a mean giraffe. But her soft voice gave the controller trouble and slowed her on the Stroop test. “My brain age is 70!” she wailed. Unfortunately for my flagging sense of pride, that did not last long. She soon scored “younger” than I, and the brain age arms race was on.

After a week of exercises such as Low to High, Calculations $\times 100$, and Head Count, were my synapses any slicker? It is hard to say, when there is no external yardstick against which to measure progress. But one week into brain training, while taking a phone message, I found I could effortlessly hold one 10-digit number in my head and scribble down another. Maybe Kawashima is onto something.

Heart of Smartness

When you hold information like a phone number in your head, you are using short-term memory, a key tool that the brain uses in processing speech. Short-term memory also comes into play in another learning game I tried, because it is a problem area for many people who struggle with mental disabilities. “I see children, adolescents and adults with various conditions



all the way through cognitive dysfunction to brain injury,” says Patricia Chunn, a clinical speech pathologist. “For many of these people, the biggest problem is memory.” Chunn is scientific adviser to Learning Enhancement Corporation, a Chicago-based company. In July 2005 LEC released BrainWare Safari, software that is designed to improve cognition and memory in children aged 6 to 12. Safari, like Brain Age, knits logic puzzles and memory challenges into a gamelike setting. In Safari, however, the quest is for an *older* brain. You choose an animal—a monkey, jaguar, parrot or bear—who starts off as a toddler. The goal as you complete levels is to help your avatar friend grow up to be an adult, with business suit and briefcase.

To use Safari, you must connect to the Internet. My trial username and password were regis-

Neuroscientist Ryuta Kawashima exhorts players in Nintendo's Brain Age (left). Rather than using a joystick, users scrawl answers (above).

(The Author)

KASPAR MOSSMAN is a Ph.D. candidate in biophysics at the University of California, Berkeley. The last computer game he owned was Crystal Quest for the Macintosh Plus.

BrainWare Safari challenges kids to take a variety of tests with jungle themes.



Positive reinforcement is relentless.
“You have succeeded at this challenge!”

tered to my editor. I did not realize this mattered until I chose Moby Monkey and finished my first task, picking out a geometric shape that did not fit in a lineup. Moby skittered onto the screen in his diapers. “Good for you, Mariette!” Then he scampered back into the bush. My first thought: “I have to get that primate out of those ridiculous Pampers pronto.” My second: “If I fail any of these tests, at least it won’t be me who looks dumb.”

It is difficult to imagine what the average cyber-savvy eight-year-old would think of Safari’s somewhat clunky graphics. The home screen is a Peruvian panorama with volcanoes, Inca ruins, llamas and various jungly inhabitants depicted in bright colors. As you move your cursor around, cartoon blurbs pop up, challenging you to take tests such as Volcanic Patterns and Piranha Pass. In the center is the Safari Lodge, where I went to check how many tests remained before I could get Moby into some trousers. I quickly identified what did not belong inside the Andean hut: the Safari Guide, an explorer in khaki with a bristly mustache.

Shown a string of colored boxes and instruct-

ed to click five times to the beat before repeating the sequence, I belatedly realized there was a soundtrack. I found that recalling colors was much harder if I first had to match the rhythm. “Clicking forces [the processing task] into short-term memory,” Chunn says. Safari (\$349 for the first user, \$200 for the second, \$150 for others) was carefully planned and is under constant revision: psychologists, vision therapists and speech pathologists advise the designers. Positive reinforcement is relentless. “You have succeeded at this challenge!” “You should be very proud!” The comments quickly became too much, and I turned the sound off. But it is important to children, says Betsy Hill, LEC’s vice president of marketing. “They get so excited when their character changes or the fireworks go off.” LEC plans to introduce a version for adults soon. BrainWare Vegas, anyone?

Get Your Motor Runnin’

Research also provides the foundation for Smart BrainGames, made by CyberLearning



Technology in San Marcos, Calif. Compared with Brain Age and BrainWare Safari, Smart BrainGames feels like pure play—although it, too, is play with a purpose. It is intended for children with attentional difficulties or patients recovering from brain injuries such as concussions. The user plays a racing game on a Sony PlayStation while wearing electrodes to monitor brain waves. The object is to keep your brain waves calm while you zoom down the freeway, dodging slowpokes.

For Smart BrainGames (\$584), CyberLearning licenses a NASA patent on using electroencephalographic feedback to modify a video game during play [see “Train Your Brain,” by Ulrich Kraft; *SCIENTIFIC AMERICAN MIND*, February/March]. I met Domenic and Lindsay Greco, co-founders of CyberLearning, at the Serious Games Summit in San Jose, Calif. Domenic explained about alpha, beta and theta waves—different low-frequency voltage oscillations that the brain produces—while Lindsay soaked three electrodes in electrolyte solution. The ratio of beta to alpha and theta waves produces what NASA calls the Engagement Index, a measure of attention to the task. The target mode corresponds to a range of this index. If you get too excited and your brain waves stray outside, you start to lose steering control and power.

Lindsay attached the electrodes, fitted into a visor: one behind my ear, one on the top of my head and one on my left temple. “With traditional neurofeedback devices,” Domenic said, “you have to sit with the patients and motivate them.” You do not need much encouragement



with Smart BrainGames. I fired up my engine and accelerated onto the freeway. Suddenly, the handheld controller vibrated, another form of feedback. “See, you just lost steering,” Domenic said. The car drove sluggishly. I strained to relax my brain waves, but no dice. The car slipped in and out of control. Bam! I rear-ended a van at 125 mph, and the car, windshield shattered, spun 360 degrees. I just did not have a feeling for what was needed.

“What you’re trying to do is create conscious correlations—‘What am I doing that’s having that dramatic effect?’” Domenic added. “You’ll get that as you work with the system on a more regular basis.” In other words, I was trying too hard to feel an active connection between my brain and the game. According to Domenic, if I played Smart BrainGames for two weeks, my brain would find its way by trial and error into a state akin to that experienced by quarterback Joe Montana at the height of his powers.

I left the Serious Games Summit without having felt the mind-machine connection. Nevertheless, driving home in heavy traffic, I saw that crash over and over again in my mind, from all angles. I concentrated as hard as I could to keep my brain waves in the zone. **M**

The author struggles heroically to get his brain in the zone (left). The task: race this hot rod (above) without losing your cool.

(Further Reading)

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- ◆ **The Better Brain Book.** David Perlmutter and Carol Colman. Riverhead, 2004.
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- ◆ **www.happyneuron.com**, a Web resource for mental fitness.

Outside the Sandbox

Parents and teachers have many options to encourage children to think creatively **BY SIMONE WELZIEN**

WHAT IS THE BEST approach to solving a problem? From kindergarten on, most children are taught that there is one optimal answer to any question. And that they should work logically, step by step, to reach that prize. In many cases, this tactic works. But in other situations, the newest concepts, wisest insights and most creative solutions arise only when people abandon established approaches and habitual ways of thinking. When a tire designer learns, from studying the feet of frogs, how to get the best traction on a wet road, he discovers a strategy that the mere application of logic never would have provided. Yet we are not teaching children how to solve problems in unconventional ways.

Outside-the-box thinking can be difficult to achieve in adulthood, because often it has been driven out of us over the course of our education and professional experience. Children, however, begin with a clean slate, so teachers and parents ought to challenge themselves to help them discover unusual paths. Boys and girls who grow up with this exposure will grasp new material better, retain their creativity and be ready to make the intuitive leaps that lead to great new ideas.

The Man inside the Traffic Light

During learning, our brains process information stored in the so-called cognitive maps of the cerebral cortex. These associations among neurons are very flexible, as psychologist Martha Farah of the University of Michigan at Ann Arbor demonstrated a decade ago. Farah studied how the brains of Canadian postal workers recognize letters and numbers. Normally, different regions of the cortex handle letters and numbers. But Canadian postal codes consist of a mix of these symbols, such as H3A 1Y2 in

Montreal. Sure enough, postal workers who have sorted mail for years process letters and numbers together in a single cognitive map.

The same plasticity is used when reaching outside the box. In cognitive maps, learned information is always connected with other, associated in-

formation. One strategy, therefore, is to take children out of the classroom atmosphere, for example, to visit experts in various fields. This approach has the added advantage of making learning fun; studies show that understanding is improved considerably when positive emotions are involved.

IMAGE SOURCE LIMITED/
WORKBOOK



(Amy had Manny paint a picture of the crosswalk as a bird would see it from above.)

Children will later remember what they learned because the special setting or interesting person will stick in their head. In addition, they will observe how to interact constructively with others and see the joy people feel in sharing knowledge.

Adults can find opportunities to influence a child's creative thinking simply by taking advantage of opportunities based on what a child is interested in at a given moment. For example, Manny, a four-year-old, once asked his babysitter on a trip to the store: "Who sits inside the traffic light and makes it turn red?" Amy, the 19-year-old sitter, replied spontaneously: "I don't know. Should we take a closer look?" She pulled over and had the boy wrap his arms around the light pole, so he could get a feel for its size. "There isn't room for anybody inside," Manny concluded. "Then how does it work?" Amy told Manny that once they were home they could find out.

After returning, Amy had Manny paint a picture of the crosswalk as a bird would see it from above. Meanwhile she logged on to the Internet to find out more about traffic lights and showed Manny a few pages about how they work and how they are repaired. The next day Amy called the city's transportation department while Manny stood next to the phone, to ask if anyone could perhaps show them around the repair shop. The officials agreed, and Amy and Manny had a short but educational visit.

Above all else, Manny learned through Amy's actions that it is fun to discover things and that friendly adults are willing to share interesting information. Such experts are everywhere: a mechanic at a garage who knows about engines or a tailor who does alterations and knows about applied geometry—cutting cloth in patterns that can be sewn together into square corners.

Creative Learning Ideas

WONDERS OF WEATHER

- **Build a rain gauge** out of a plastic soda bottle and take regular readings.
- **Visit a government airfield** to see the launch of a weather balloon.
- **Interview** a hurricane survivor.
- **Plant vegetable seeds** and track how temperature, water and light affect plant growth.
- **Create an alphabet** based on weather terms: Atmosphere, Barometer, Cloud ...

SOUND AND MUSIC

- **Take apart** a microphone.
- **Build a microphone** from a tin can, foil and string.
- **Visit a radio station** and watch a deejay at work.
- **Make a simple** musical instrument.
- **Visit a shop** that manufactures pianos.

Mental Gym Class

Making visits to experts or inviting them to schools and daycare centers is one means of showing kids that there are many ways, beyond books, to learn. That, in turn, encourages creative thinking.

Teachers and parents can enrich a child's day with simple but offbeat perspectives, too, which do not require new lesson plans or expensive purchases. They can present math problems during circuit training in a gym class or at a park, or play motion games during math class, or translate the rules for classroom or household behavior into French.

To learn how a lever works, kids can put a broomstick under their arms (against their chest) and experience firsthand how the force of weights hung on either end affects their own bodies. A visit to a fitness center followed by some study of the various exercise machines will make the principle of counterweights clear.

Or let kids act like machines. Have

Lisa pick up stone after stone, using the same motion each time, and pass each stone to Megan. She in turn gives it to Alex, Colin and Ben, who finally hands it to Laura, who dumps it into a bucket half full of water. After 15 or 20 stones, the water will crown and then overflow.

What have the kids learned? That a machine works best at a regular rhythm, that every cause has its effect, and that water creates a tiny meniscus at the top of a bucket because the water molecules stick to one another. (Perhaps the last point would require some adult explanation.)

Here we have engineering, physics, chemistry and physical education. If, later in life, Lisa and her friends hear about automation or surface tension, they will think back to their delightful human machine. **M**

SIMONE WELZIEN is an education consultant and a nutritionist. She founded the Thinking Out of the Box Club in Nienhagen, Germany.

Game On

"Don't Bother Me Mom—I'm Learning!"

by Marc Prensky. Paragon House Publishers, 2006 (\$19.95)

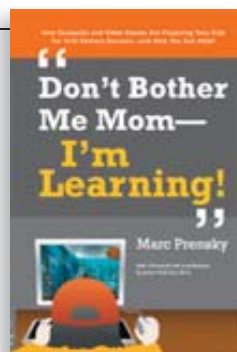
As kids spend ever more time in the virtual world, the debate over whether video games foster harmful or helpful real-world habits rages. Marc Prensky, an educational software developer, is pro-game. In *"Don't Bother Me Mom—I'm Learning!"*, Prensky maintains that kids "are almost certainly learning more positive, useful things for their future from their video and computer games than they learn in school!"

Prensky wants to ease parents' fears by describing how kids see gaming and what they learn. "[P]retty much all the information that parents and teachers have to work with is a lot of speculation, conjecture, and overblown rhetoric about the putative negative aspects of these games," he writes. Unfortunately, his counterstrategy is to throw together a similarly

speculative mix in defense.

Prensky presents an opinionated argument filled with anecdotes, a few studies, and quotes pulled from published news stories. There is no evidence too specious: he cites a recent study that found younger, newer radiologists were more accurate in reading mammograms than older, more experienced doctors and asks, "Could the higher visual acuity gained from playing video games be at work here?" How can the reader know, when Prensky didn't talk to the researchers to find out if the study was trying to answer this question?

He also takes the easy road in response to studies that find a link between aggressive behavior and violent video games: "Absolutely no one can say, when all the complex factors in a single child's life are taken into account, whether any individual child will be negatively influenced overall." Of

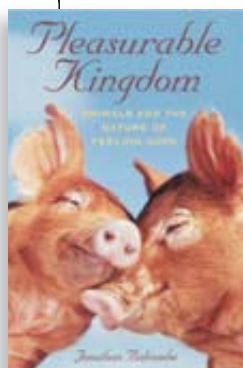


course not. The question, however, is whether video games are a risk factor for aggression and, if so, to what extent.

Nor will Prensky concede that there could be anything wrong with new technology. Writing about cell phones, he says that "the first 'educational' use

students implemented for their cell phones was retrieving information on demand during exams. Educators, of course, refer to this as 'cheating.' They might better serve their students by redefining open-book testing as open-phone testing." It is not hard to believe that children are learning problem-solving skills and hand-eye coordination from video games, as Prensky and others have written. Nor are all video games about killing things. But parents who have concerns about potential negative effects will be hard-pressed to find thoughtful, well-researched answers here. —Aimee Cunningham

Mind Reads



Pet Issue

Pleasurable Kingdom: Animals and the Nature of Feeling Good

by Jonathan Balcombe. Macmillan, 2006 (\$24.95)

If you have ever scratched a dog's belly as the animal lies, legs splayed, you would find it hard to believe that the pooch was not experiencing pleasure. Jonathan Balcombe, who has tickled many a mammal, thinks so, too, and he rails at the reductionism of biol-

ogists who see animals as genetic automatons that seek little more than to eat, sleep and reproduce. Instead, he asserts, "We are evolutionarily continuous with the other beasts ... and we are now realizing that ours is a planet rich with other minds and experiences."

Balcombe is an animal behavior research scientist with the Physicians Committee for Responsible Medicine in Washington, D.C. To back up his claim that all vertebrates, at least, experience pleasure, he presents hundreds of anecdotes about animals playing, eating, copulating, grooming, loving—and enjoying all of it. Most examples come from biologists observing or experimenting with an array of species from moles to

whales, but Balcombe also quotes pet owners and talks about his own menagerie.

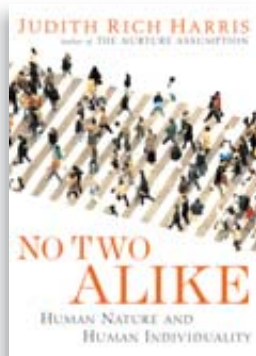
Interestingly, his best counter to the belief of some scientists that animal behavior is largely instinctual and in service of reproduction comes in his chapter on sex. In many species, only a few dominant males gain access to females, but this fact scarcely means the others abstain from sex. To the contrary, Balcombe documents the widespread practice of homosexual couplings and masturbation. The only reward for these creatures seems to be pleasure. Because animals—at least mammals—can experience both pleasure and pain, Balcombe concludes that we owe them better treatment. He ends *Pleasurable Kingdom* with a plea for improving the lives of animals, from battery hens and pigs kept in dark concrete barns to the millions of lab rats consigned to wire cages.

Unfortunately, some bad stylistic and logical choices lessen the book's impact. Balcombe lists far too many anecdotes and adds too little analysis. He also makes presumptuous leaps: the fact that birds have brilliant plumage, and eyes to see other birds' feathers, does not mean they possess an aesthetic sense. One story of a chimp supposedly watching an African sunset is turned into an epiphany in which the ape is "contented with life." Such unprovable assertions detract from an otherwise well-argued thesis. —Jonathan Beard

The Pillars of Personality

No Two Alike: Human Nature and Human Individuality

by Judith Rich Harris. W. W. Norton, 2006 (\$26.95)



Where does adult personality come from? Why are we all different? These are the questions energizing Judith Rich Harris's new book.

Harris, a former textbook author turned popular writer, dives right in, sharpening her focus by looking at identical twins. After subtracting the share contributed by their mutual genes—about 45 percent—studies show that adult identical twins are no more alike in personality than people

plucked at random from a crowd, even though the siblings were raised in the same home, by the same parents, with identical schooling.

Where, then, do personality differences come from? Harris begins, in a savage fashion familiar to readers of her *Nurture Assumption*, by recounting factors that do *not* contribute to personality differences. She debunks dozens of studies by psychologists—especially the “developmentalists” and “interventionists” who believe that better parenting or school environments can affect how children turn out—by pointing out where they have fudged numbers and twisted results. She rejects the basis of psychoanalysis, stating there is no evidence that talking about childhood experiences has therapeutic value. She also maintains that learned behaviors do not readily transfer from one situation to another, noting that even babies behave differently to fit different environments.

To answer her opening questions, Harris then develops a complex scheme based on “the modular mind,” a framework set forth by Harvard University evolutionary psychologist Steven Pinker and others. (Harris herself has no doctorate and is housebound by systemic sclerosis and lupus, two autoimmune disorders.) She describes three modules—the relationship system, the socialization system and the status system—and explains how each contributes its part to making us who we are. The relationship system starts in the cradle as infants study and learn the faces and voices of the people around them, collecting information that helps form personality. The socialization system adapts people to their culture. The status system takes all the information collected during childhood and adolescence and shapes and modifies our personalities in accord with our environments.

Harris's last chapter lays out her theory in tabular form, explaining how each module interacts with the others to produce our distinct personalities. It is lavishly footnoted, like the rest of the book, shoring up her strategy of pointing out the failings of other models and then proposing her own. Her goal, she writes, is to explain the variations in personality that cannot be attributed to variations in people's genes. After saying she believes she has succeeded, she throws down her gauntlet: “I will leave it to other people to test my theory.”

—Jonathan Beard

Tough on Tough Love

Help at Any Cost: How the Troubled-Teen Industry Cons Parents and Hurts Kids

by Maia Szalavitz. Riverhead Books, 2006 (\$25.95)

In 1958 a residential treatment program for heroin addicts, called Synanon, initiated a radical methodology to break the addiction cycle. Using “attack therapy” in an environment of “tough love,” counselors forced drug users to alter their self-destructive behaviors. Such methods became so popular that in 1982 counselors Phyllis and David York argued in their best-seller *Toughlove* that families should also embrace harsh measures. Hundreds of tough love–style residential programs have since emerged. Yet no scientifically supportable evidence has ever shown that these methods are effective. In fact, some data suggest they may do harm.

In *Help at Any Cost*, Maia Szalavitz, a senior fellow of the Statistical Assessment Service at George Mason University, shows how “abusive, dehumanizing practices that reformers of mental hospitals and prisons have attempted to stamp out for centuries” have

been repackaged and sold to desperate parents. “Thousands of well-meaning, caring, and intelligent parents have been taken in by a business that uses exaggerated claims of risk to teens to sell its services.” All of this has amounted to a multibillion-dollar industry. This is a story, she says, “of splintered families; of parents convinced by program operators that extreme, even traumatically stressful treatments are their children's only hope.”

Homing in on several leading programs, Szalavitz carefully documents cases of reckless punishment that physically and psychologically hurts youths. Military-style boot camps and wilderness programs that pursue extreme “rehabilitation” measures have left teens dead of illnesses and dehydration, spawning numerous lawsuits. Such “professional” programs operate nationally and charge college-equivalent tuitions. Yet there is no regulatory oversight or medical or legal evaluation of the quality, competency or effectiveness of such programs, even though they assume responsibility for the lives of minors.

Citing a draft consensus report by the U.S. National Institutes of Health, among other studies, Szalavitz says such programs simply do not work. The evidence that exists “offers no reason to believe that group detention centers, boot camps, and other ‘get tough’ programs do anything more than provide an opportunity for delinquent youth to amplify negative effects on each other.”

Szalavitz concludes her book gently with practical guidance for parents of troubled teens, including ways to get more sophisticated help. Ultimately, she urges parents not to yield to desperation and to recall the leading principle of medical ethics: “First, do no harm.”

—Richard Lipkin



asktheBrains

Why do some expectant fathers experience pregnancy symptoms such as vomiting and nausea?

—D. Barrera, McAllen, Tex.

Katherine E. Wynne-Edwards is a professor of biology at Queen's University in Kingston, Ontario, who studies hormonal changes in expectant fathers. She answers:



MANY FACTORS—from social to hormonal—could play a role when an expectant father experiences typical pregnancy side effects such as nausea, weight gain, mood swings and bloating. The condition is called *couvade*, from the French verb *couver*, which means “to hatch” or “to brood.” Across a wide range of studies—and an equally wide range of definitions of what constitutes *couvade*—estimates of the frequency of *couvade* range from less than 20 percent to more than 80 percent of expectant fathers.

Only recently has this phenomenon received attention from scientists, spawning a variety of hypotheses. Because a couple may experience lifestyle changes together, the cravings and increased appetite of a pregnant wife may pave the way for her husband's weight gain, heartburn and indigestion. Conversation at home can range from frustrated incapacitation to boundless anticipatory joy, fostering jealousy of the ability to carry a child, guilt over having caused this transformation in his partner and selfish attention seeking. Changes in sexual activity, shifts in social priorities, time off work, or the arrival of a mother-in-law for a potentially stressful extended visit may also contribute.

Some studies suggest that men who have deep empathy toward their pregnant partner and who are prone to *couvade* symptoms end up with strong attachments to their child. If this is the

case, the symptoms might either stimulate or result from underlying biological processes that are involved in social attachment.

Recent studies also have shown that some of the same hormones that fluctuate for pregnant women are also affected in future fathers. Men with higher levels of prolactin, which causes lactation in women, report more *couvade* symptoms. Paternal prolactin causes a decrease in testosterone and sperm production and peaks just before delivery. Levels of cortisol (a steroid hormone secreted in response to stress) and the sex steroids estradiol and progesterone also change in the father, though not as much as do those in the mother.

Unfortunately, we do not know yet whether current connections between hormonal changes and behaviors are cause-and-effect patterns or just correlations. No doubt testosterone concentration is lower in men in relationships, for instance, but it is unclear whether men have a decrease in testosterone after the relationship begins or whether men with lower testosterone are more likely to enter into stable relationships. It is tempting to look to hormones as the biological root of *couvade*, but other social and emotional factors could be equally influential. Either way, questions in this area have quietly expanded the horizons for research on male hormone levels—testosterone alone is clearly no longer the sum of the man.

Why can't you tickle yourself?

—T. Bogaerts, Lebanon, Tenn.

Sarah-Jayne Blakemore, a research fellow at the Institute of Cognitive Neuroscience at University College London, responds:



THE ANSWER LIES at the back of the brain in an area called the cerebellum,

When you try to tickle yourself, the cerebellum predicts the sensation, and this prediction is used to cancel the response of other brain areas to the tickle.

which is involved in monitoring movements. Our studies at University College London have shown that the cerebellum can predict sensations when your own movement causes them but not when someone else's does. As a result, when you try to tickle yourself, the cerebellum predicts the sensation, and this prediction is used to cancel the response of other brain areas to the tickle.

Two brain regions are involved in processing how tickling feels. The somatosensory cortex processes touch, and the anterior cingulate cortex processes information related to pleasurable sensations. We found that both these regions are less active during self-tickling than they are when someone else is doing the poking. This fact helps to explain why tickling ourselves does not feel tickly and pleasant.

Studies using robots showed that having a small delay between your own movement in starting the tickling motion of the machine and the resulting prod can make the sensation feel tickly. Indeed, the longer the delay, the more tickly it feels. So it might be possible to tickle yourself, if you are willing to buy a couple of robots. **M**

Have a question? Send it to editors@sciammind.com

COURTESY OF KATHERINE E. WYNNE-EDWARDS (top)

Head Games

Match wits with the Mensa puzzler

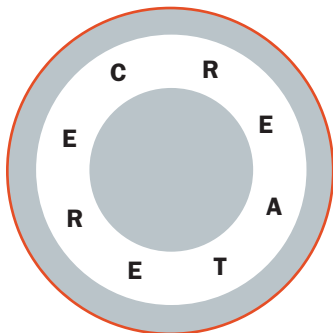
BY ABBIE F. SALNY

1 Rearrange the same five letters to form two different words that work in the sentence below.

The _____ at this hotel are so high, I had to _____ at my bill for some time before I could believe it.

2 Add an "r" to a word that describes a "geographic feature" to create a word that means "something to put over an object."

3 An eight-letter word is coiled in the circle below. Start at the correct letter and move clockwise or counterclockwise to find the word.



4 Name one additional letter that lets you make four words out of the three letters below (using each letter only once). (Good for you if you find a second answer!)

I T E

5 The peculiar grocer on the corner charges some unusual prices. A cucumber costs 11¢, a tomato costs 9¢ and a pumpkin costs 9¢. Using the same logic, how much does a squash cost?

6 What is the five-digit number in which the third and fourth number are the sum of the first and second, the first is one less than the second, the last is one less than the fourth, the second is seven more than the third and the sum of all the digits is 25?

7 Find the names of two colors hidden in the sentences below. The letters are in alphabetical order.

I altered the original papers.
The sharp ink marks were easy to eradicate.

8 What word logically belongs in the first set below?

bland blink braid bone

braille

blue

bang

band

9 Rearrange the following letters to form a cynical five-word phrase about doing the right thing.

EEEEIOOOOUUDDDDGGHNNNPSS

10 Fill in the grid below so that you have a total of one M and one D; two T's, N's, R's and I's; and three A's and E's. Each line contains a word that can be read across and down.

M	I	N	T
I			
N			
T			

Abbie F. Salny, Ed.D., was the supervisory psychologist for American Mensa (www.us.mensa.org/sciamm) and Mensa International (www.mensa.org) for more than 25 years. She is the author and co-author of many challenging puzzle books, including the Mensa Think-Smart Book and the Mensa 365 Brain Puzzlers Page-A-Day Calendar (Workman Publishing).

Answers

T	A	R	E
N	E	A	R
I	D	E	A
M	I	N	T

10.

1. Rates, stare.
2. Cove, cover.
3. Recreate.
4. Use "m," to spell emit, time, mite and item. Or use "d" to spell diet, tide, edit and dite.
5. 8¢. (2¢ per vowel, 1¢ per consonant.)
6. 78,154.
7. Red, pink.
8. Band. (The last three letters of each member of the set form a three-letter word.)
9. No good deed goes unpunished.

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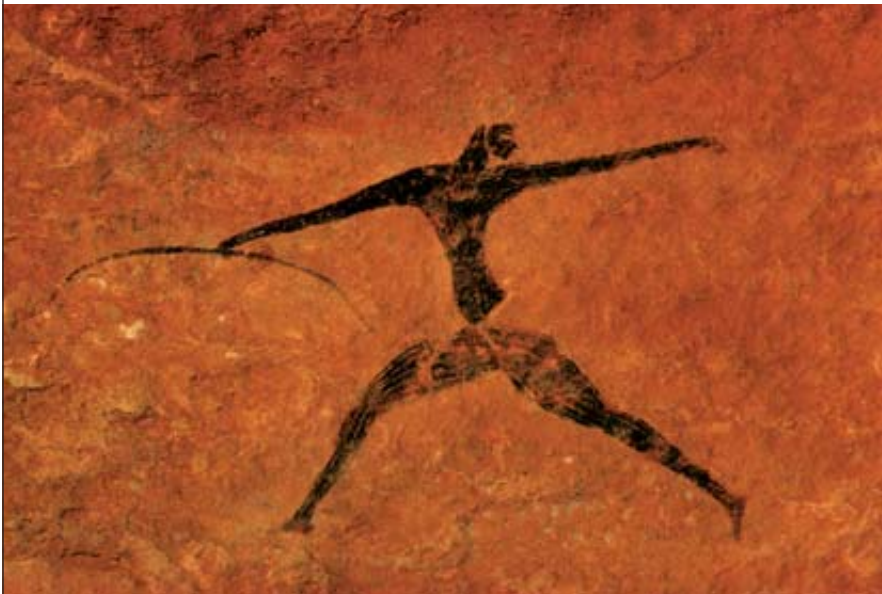
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